

ABSTRACTS OF WORLD MEDICINE



University Of Alabama
Medical Center

AUG 28 1961

Library

A Monthly Critical Survey
of Periodicals in
Medicine and its Allied Sciences

LONDON
BRITISH MEDICAL ASSOCIATION
TAVISTOCK SQUARE, W.C.1

Copyright © 1961

YEARLY SUBSCRIPTION £4.4.0

U.S.A. AND CANADA \$13.50

SINGLE NUMBER 8/6

ABSTRACTS OF WORLD MEDICINE

UNDER THE DIRECTION OF

HUGH CLEGG, M.A., M.D., F.R.C.P., Editor, *BRITISH MEDICAL JOURNAL*

EDITOR

DONALD CROWTHER, B.A., B.M., B.Ch.

ASSISTANT EDITOR

A. DEWAR DUFF, M.B., Ch.B.

SUB-EDITOR

MARJORIE H. HOLLOWELL

It is the aim of this journal to provide the reader with abstracts of all important articles appearing in medical periodicals published in every part of the world, and in this way to enable him to keep in touch with new developments throughout the whole field of medicine and in each of its special branches, including those aspects of surgery which are of particular concern to the physician.

More than 1,600 periodicals are surveyed, from which are selected for abstracting those papers which appear to make some useful contribution to the sum of medical knowledge or experience. Each paper is abstracted in sufficient detail to indicate to the general reader the nature and value of that contribution and to enable the specialist to assess its importance in relation to his own work and to decide whether the original article should be read in full. The author's own summary or an editorial summary published with the original article may occasionally be reproduced if it is suitable for these purposes, and the title and reference alone may be published in order to draw attention to a review article or other type of paper which cannot readily be abstracted.

The abstracts in each issue are grouped in sections according to subject and, so far as possible, those dealing with medical and surgical aspects of the same problem appear together. The titles of papers written in languages other than English are given both in translation and in the original form. The titles of journals are given in full and also abbreviated according to the rules adopted in the *World List of Scientific Periodicals*, as modified by *ISO Recommendation R4: International Code for the Abbreviation of Titles of Periodicals* (International Standards Organization, 1957), and in *World Medical Periodicals* (Second Edition, World Medical Association, 1957). The transliteration of authors' names from the Cyrillic alphabets is in accordance with *ISO Recommendation R9: International System for the Transliteration of Cyrillic Characters* (International Standards Organization, 1955).

Explanatory or critical comments by the abstracter or editor are enclosed within square brackets.

ABSTRACTS OF WORLD MEDICINE

VOL. 30 No. 2

AUGUST, 1961

Pathology

264. **The Differential Diagnosis between Myocardial and Pulmonary Infarction by the Estimation of Serum Enzyme Activity.** (Die Differentialdiagnose zwischen Herz und Lungeninfarkt durch Bestimmung von Fermentaktivitäten im Serum)

D. KLAUS and E. ZEH. *Deutsche medizinische Wochenschrift [Dtsch. med. Wschr.]* 86, 480-483, March 17, 1961. 22 refs.

In 9 out of 12 patients with pulmonary infarction investigated at the University Medical Clinic, Tübingen, the levels of both serum glutamic-oxalacetic transaminase (G.O.T.) and glutamic-pyruvic transaminase (G.P.T.) were raised, the latter more than the former, while serum lactic dehydrogenase (L.D.H.) activity was raised in 6 of 7 patients investigated, the absolute number of units being greater than for G.O.T. or G.P.T. The level of isocitric dehydrogenase (I.D.H.) was raised in 10 of 12 patients and that of malic dehydrogenase was greatly raised in 3 out of 4. On the other hand leucine aminopeptidase activity was only slightly raised in 2 of 5 patients. In general, enzyme levels were highest on the day of the infarction and fell rapidly, that of G.O.T. falling faster than G.P.T. There was good correlation between the clinical severity of the disease and the serum enzyme levels. The authors point out that the increase in serum L.D.H. and G.P.T. levels which occurs only in pulmonary infarction serves to distinguish this condition from myocardial infarction, in which the main rise is in G.O.T. and L.D.H. levels. The finding of normal enzyme values, however, does not exclude pulmonary infarction.

M. Lubran

EXPERIMENTAL PATHOLOGY

265. **The Site of Formation of Haematopoietic Substances.** (О месте образования гемопоэтических веществ)

N. A. FEDOROV, M. G. KAHMELIDZE, and I. K. KORJAKINA. *Проблемы Гематологии и Переливания Крови [Probl. Gemat.]* 5, 17-21, Nov., 1960. 1 fig., 42 refs.

It is now known that in various hypoxic states substances appear in the blood capable of stimulating erythropoiesis in normal and anaemic animals, but so far the site of the formation of these substances has not been definitely established. This problem was therefore studied in 15 series of controlled experiments on rats, from which various organs were removed singly or in

combination and production of the haematopoietic factor stimulated by the withdrawal of blood up to 1-5% of the animal's body weight. The haematopoietic activity of the serum was determined 20 to 24 hours later by means of a haemoculture technique based on the ability of the haematopoietically active substances to enhance migration of leucocytes. In two further series of controlled experiments the haematopoietic activity of the serum was studied before and again 24 hours after blood letting (2% of body weight) in 12 rats 11 to 60 days after gastrectomy. The results were evaluated statistically.

The mean increase in haematopoietic activity of the serum after blood loss in 56 control animals was +30%. In the experimental groups the mean changes in serum haematopoietic activity, expressed as a percentage of the control values, after the removal of various organs was as follows: gastrectomy -60%, splenectomy +73%, gastrectomy plus splenectomy -27%, bilateral nephrectomy -83%, unilateral nephrectomy +17%, and after bilateral ligation of the ureters -73%. The results of the two series of chronic experiments showed that gastrectomy in rats resulted in disappearance of the haematopoietic factor from the blood and that the capacity to form the factor in response to acute blood loss was also lost. It is concluded that the stomach is the site of formation of the haematopoietic factor, while the spleen has an antagonistic effect on the haematopoietic activity of serum. The effects of nephrectomy and ureteric ligation being similar, the loss of haematopoietic activity may have been the result of the consequent uraemia.

S. W. Waydenfeld

266. **The Effects of Blood Phosphatides on Haematopoiesis.** (Влияние фосфатидов крови на гемопоэз) A. A. RAKITJANSKAJA and S. S. HARAMONENKO. *Проблемы Гематологии и Переливания Крови [Probl. Gemat.]* 5, 21-26, Nov., 1960. 4 figs., 13 refs.

The haematopoietic activity of the serum is increased in anaemias associated with haemolysis and also after blood loss and blood conditions in which haemolysis is a probable underlying factor. Of the various products of disintegration of erythrocytes, phosphatides appear to be responsible for this effect. In the present experiments 18 healthy dogs and 11 dogs from which 20 to 80 ml. of blood was withdrawn daily for 40 to 100 days were given intravenous injections of a 4% emulsion of iso- or heterophosphatides in saline.

With both forms of phosphatides leucocytosis developed within 5 minutes and the leucocyte count continued

to rise for the next few days. A single injection of phosphatides (0.1 to 0.5 ml. per kg. body weight) was followed after 1 or 2 days by a 5 to 12% increase in haemoglobin concentration and a rise of 500,000 to 1,500,000 per c.mm. in the erythrocyte count. In dogs with high initial values there was no increase in the haemoglobin level, but a marked rise in the number of polychromatophil cells. In those with low initial haemoglobin values and erythrocyte counts the resulting increase lasted for 20 to 25 days. If large doses of phosphatides were given the initial rise in haemoglobin concentration and erythrocyte count was followed by a fall; at the same time, however, there was erythroblastic hyperplasia of the marrow with predominance of basophilic elements, the result being a hypochromic anaemia with polychromatophilia which persisted for 6 weeks or more. The haematopoietic effect of phosphatides was demonstrated in animals in which experimental anaemia was produced by small repeated bleedings. Phosphatide therapy was started when the haemoglobin concentration had fallen to 25 to 35% and the erythrocyte count to 3,000,000 to 3,500,000 per c.mm. Injections of phosphatides (0.17 to 1.2 ml. per kg.) were given every 3 or 4 days. Whereas treated animals recovered in 14 to 23 days, the controls remained apathetic, continued to lose weight, and their trophic lesions did not heal for 35 to 40 days. The bone marrow of the experimental animals showed much more activity. When the blood loss was more severe the effects of phosphatide therapy were less evident.

It is concluded that the haematopoietic activity of phosphatides is the active factor concerned in so-called haematopoietic serum and also in the greater haematopoietic effect of stored blood as compared with fresh citrated blood, since in the latter only small amounts of the products of haemolysis are present.

S. W. Waydenfeld

267. Mechanism of Arterial Hypertension. Role of Capacity and Resistance Vessels

M. A. FLOYER and P. C. RICHARDSON. *Lancet* [*Lancet*] 1, 253-255, Feb. 4, 1961. 2 figs., 8 refs.

Experiments were carried out on parabiotic rats at the London Hospital to demonstrate the relationship between sodium excretion and plasma volume and the blood pressure. From the results of these experiments the authors consider that arterial hypertension may result not from an increase in arteriolar resistance, but from a disturbance of the normal relationship between the tone of the capacity vessels and the volume of their contents.

In order to test their hypothesis a renal artery in one member of 14 pairs of parabiotic animals was partially occluded by a silver clip. The blood pressure of both animals rose, but was always higher in the "clipped" animal. Moreover, although the plasma volume rose in each member of the 4 pairs in which it was measured, the rise was always less in the animal with the constricted renal artery than in its partner. This redistribution of blood indicated that constriction of the renal artery produced an increase in capillary blood pressure in the animal with the clipped vessel. This is attributed to an increase in tone of the capacity blood vessels relative to the blood volume.

J. B. Wilson

MORBID ANATOMY AND CYTOLOGY

268. Rheumatic Phlebitis of the Coronary Veins

W. C. VON GLAHN and M. KUSCHNER. *American Journal of Pathology* [*Amer. J. Path.*] 38, 251-261, Feb., 1961. 6 figs., 12 refs.

Writing from Louisiana State and New York University Schools of Medicine, the authors briefly review the literature of rheumatic phlebitis. They then describe a type of lesion of the coronary sinuses found in cases of active rheumatic heart disease. The material used consisted of 19 histological sections from 18 cases of active rheumatic heart disease which included the coronary sinus. This was compared with comparable material from 35 individuals without evidence of rheumatic disease.

Of the 18 cases of rheumatic disease, lesions were present in the coronary sinus in 10. An acute inflammatory reaction of the sinus was found in 8 cases, in 5 of which Aschoff bodies were also present in the adventitia. Aschoff bodies were seen in the adventitia without other reaction in one case. In 3 cases there were bands of eosinophilic material in the intima and an acute inflammatory reaction with Aschoff bodies in the adventitia. The lesions involved only sectors of the sinus wall and in structure closely resembled those of rheumatic endocarditis. No thromboses were present. Healed lesions were seen in 5 cases, in 4 of which there were also acute lesions. The phlebitis apparently developed and healed rapidly and the presence of acute and healed lesions in the same sinus indicated that the vessel was being damaged repeatedly. In none of the control cases were similar lesions seen.

R. Wyburn-Mason

269. Endocardial Thickening Associated with Diseased Valves

W. J. S. STILL. *British Heart Journal* [*Brit. Heart J.*] 23, 155-160, March, 1961. 11 figs., 7 refs.

In an endeavour to determine the pathogenesis of the endocardial thickenings and pockets that are found in relation to the valvular lesions in aortic valvular disease 10 cases of aortic stenosis and 2 cases of adult subaortic stenosis were examined histologically at the Royal Free Hospital, London.

The author concludes that the endocardial pockets are built up from mural thrombus deposited on the endocardial wall, damage to the wall being caused by the distorted jet of blood. While endocardial pockets tend to form below the aortic valve, endocardial thickening is the main feature of the changes in the aorta above the valve.

J. B. Wilson

270. Paneth Cell Metaplasia in Ulcerative Colitis

J. C. PATERSON and S. H. WATSON. *American Journal of Pathology* [*Amer. J. Path.*] 38, 243-249, Feb., 1961. 3 figs., 13 refs.

At the Westminster Hospital, London, Ontario, estimates of the numbers of Paneth cells in the mucosa of the colon removed in 10 cases of ulcerative colitis with a duration of symptoms varying from 1 to 20 years were made. These were compared with those in 10

"normal" colons. In the former group the number of crypts showing the presence of these cells varied from 0.6 to 30% (average 19.6%). The incidence was correlated with the clinical duration of the disease except in one case. These findings were in marked contrast to the frequency with which Paneth cells were found in the crypts in the control series, in which the average incidence was only 0.3%. In the cases of ulcerative colitis the Paneth cells were usually found in areas which were interpreted as regenerated or previously damaged mucosa. None were seen adjacent to areas of recent ulceration. The authors interpret their presence as a metaplastic change and the result of chronic inflammation.

R. Wyburn-Mason

271. Gastro-oesophageal Carcinoma of Mixed Histological Type

O. G. DODGE. *Journal of Pathology and Bacteriology* [J. Path. Bact.] 81, 459-471, 1961. 13 figs., 27 refs.

In the Department of Pathology, University of Sheffield, 7 cases of gastro-oesophageal carcinoma of mixed histological type were found in the course of a study of 87 surgically excised carcinomata of the gastro-oesophageal region.

Three possible theories to account for the occurrence of these mixed tumours are discussed. The mixed pattern may be the result of squamous metaplasia in gastric adenocarcinoma. This is believed to have occurred in 2 cases. Alternatively, the tumour may arise from distinct types of epithelium lying within a single field, a carcinogenic stimulus invoking a neoplastic response in the cells of two adjacent but different types of epithelium. Three criteria are set out for the diagnosis of dual histogenesis in cases of mixed gastro-oesophageal carcinoma:

"(1) the two structural components (squamous and glandular) should show at least partial topographical separation; (2) the areas of squamous differentiation should lie, on the whole, to the oesophageal side of the tumour, and the areas of glandular differentiation to the gastric; (3) there should be little or no evidence of intermediate histological structure". Three cases are classified in this group, 2 showing partial segregation of their two component patterns and the third being a clear example of a "collision tumour". The latter is defined as the concrescence of two independently arising neoplasms of different histological patterns, the two types of growth being clearly separate in the metastases also. The third possible origin is from oesophageal mucous glands or their ducts. Two cases were considered to be of this origin. They showed areas of typical mucoepidermoid pattern and smooth transitions between this and the squamous and glandular areas. H. Caplan

272. Amyloid Disease of the Bone Marrow: Diagnosis by Sternal Marrow Aspiration

R. B. CONN JR. and R. D. SUNDBERG. *American Journal of Pathology* [Amer. J. Path.] 38, 61-71, Jan., 1961. 4 figs., 19 refs.

Involvement of the bone marrow in generalized amyloidosis is thought to be relatively uncommon and is rarely recognized except at necropsy. In the past 4

years the authors, at the University of Minnesota Hospitals, Minneapolis, have encountered 3 cases of primary amyloidosis in which amyloid was found in films and sections of bone marrow obtained by aspiration biopsy.

A review of marrow biopsy specimens previously obtained from patients with known or suspected amyloidosis revealed amyloid which had been unrecognized initially in 2 cases. In both cases marrow films showed no amyloid, but in sections this was demonstrated in the walls of the medullary vessels. Amyloid was also found in 8 of 9 cases of amyloidosis examined at necropsy; in 7 of these there was limited vessel involvement and in one the bone marrow was extensively replaced.

In marrow films stained with Wright's stain amyloid appeared as a structureless, homogeneous, purple-to-pink-staining, waxy material occurring in masses among the marrow cells. The differentiation of amyloid from non-specific precipitated protein presented little difficulty, although small accumulations of amyloid could mimic the cytoplasm of a ruptured megakaryocyte. Metachromasia with crystal violet varied in degree from area to area in the same preparation. All the amyloid was strongly positive with the periodic-acid-Schiff (P.A.S.) stain. A useful procedure was treatment of the tissue with ptyalin, which resulted in a much weaker reaction to the P.A.S. stain in platelets and megakaryocytes, while the reaction in amyloid remained unchanged. The amyloid deposit first appeared in the small vessels of the medullary cavity and then spread into adjacent haematopoietic tissue, finally replacing much of the marrow. A consistent finding in both primary and secondary amyloidosis was a slight to moderate increase in plasma cells. Russell bodies were found in the plasma cells in both forms of the disorder.

A. W. H. Foxell

273. Pulmonary Metastases Imitating Alveolar-cell Carcinoma

P. ROSSMANN and V. VORTEL. *Journal of Pathology and Bacteriology* [J. Path. Bact.] 81, 313-321, 1961. 16 figs., 23 refs.

The authors, writing from the Institute of Pathology of the Medical Faculty of Charles University, Hradec Králové, Czechoslovakia, report 5 cases of primary adenocarcinoma arising outside the lung and giving rise to extensive pulmonary intra-alveolar metastases mimicking the so-called alveolar-cell carcinoma. The primary tumours arose in the pancreas, ascending colon, rectum, breast, and thyroid gland respectively.

The literature is reviewed and the criteria given by various authors for the diagnosis of primary alveolar carcinoma are discussed. Many different macro- and microscopic patterns have been described. The tumour might be uni- or multicentric or generalized. The histological pattern might be alveolar (mural), diffuse (pneumonic), or mixed. The neoplastic cells described ranged from highly uniform columnar cells to low, cuboidal, anaplastic, or dissociated elements. In some cases lymphatic permeation is described, while other authors stress its absence. The tendency of the cells to grow and disseminate upon the preformed lung tissue without forming any proper interstitial stroma is usually con-

sidered the essential distinction from the ordinary destructive adenocarcinoma. However, the authors quote a case in which metastases spread in the branches of the portal vein in an exclusively "alveolar" manner without any trace of invasion of the hepatic tissue.

All the features mentioned as characteristic of primary alveolar-cell carcinoma could be found in one or more of the original cases described here, all of which were certainly metastatic in origin. This supports the view of Ech that "in all cases in which no tumour can be found outside the lungs there exists a small invasive carcinoma, perhaps very difficult to detect, at some point within the lungs, and that the apparent alveolar-cell carcinoma is derived from this primary".

H. Caplan

274. The Metastatic Origin of Alveolar-cell Tumour of the Lung

T. F. HEWER. *Journal of Pathology and Bacteriology [J. Path. Bact.]* 81, 323-330, 1961. 12 figs., 5 refs.

From the Department of Pathology, University of Bristol, the author reports 4 cases of apparent alveolar-cell carcinoma of the lung which proved to be examples of pulmonary metastases of carcinomata originating in the pancreatic duct. This finding led to a review of 64 consecutive examples of primary carcinoma of the pancreas in the records of the department. Pulmonary metastases were noted in 10 cases, in 3 of which there was undoubted extension along the alveolar wall. Thus there were 5 cases of this type in a series of 66 carcinomata of the pancreas. A review was then made of 78 examples of metastatic pulmonary tumours derived from sites other than the pancreas and in 3 cases (carcinomata of the stomach, ovary, and breast respectively) there was spread along the alveolar wall of sufficient degree to warrant consideration of an alveolar-cell origin.

It is concluded that the picture of alveolar-cell carcinoma (a term which is often used as synonymous with pulmonary adenomatosis) can be produced by metastases of a variety of well differentiated, columnar-cell, mucus-producing carcinomata and that all cases so reported are in reality either metastases from an extrapulmonary site or extensions of a bronchial carcinoma. In cases of chronic irritation of lung tissue, where there is manifest epithelial hyperplasia in the alveolar walls, the picture is easily differentiated from the neoplastic condition under consideration.

H. Caplan

275. Exfoliative Cytology of Pleural, Peritoneal and Pericardial Fluids

J. W. REAGAN. *CA. Bulletin of Cancer Progress [CA. (N.Y.)]* 10, 153-159, Sept.-Oct., 1960 [received Feb., 1961]. 6 figs., 47 refs.

Cytological studies of pleural, peritoneal, and pericardial fluids are carried out to gain knowledge of the aetiology of the transudate or exudate. This paper from Western Reserve University and University Hospitals, Cleveland, Ohio, gives a short review of the history of the subject and its techniques, followed by an analysis of the results of such studies over a period of 28 years in a series of cases in which necropsy was subsequently

performed. A total of 673 fluid samples were examined from 369 patients, of whom 207 had a malignant tumour and an effusion in one or more of the body cavities. In 153 (73.9%) of these cases demonstrable tumour cells were present in one or more fluid samples examined before death. There was one case in which malignant cells were found in the fluid but no cancer was found at necropsy. Of 162 patients in whom no malignant tumour was found at necropsy, 161 had no cytological evidence of cancer. However, of the samples which were reported as not containing malignant tumour cells, 25.1% proved to be from patients with effusions related to malignant neoplasms. A negative report therefore does not exclude the presence of such a neoplasm, even when the examination is in experienced hands. The ability to demonstrate malignant cells in serous effusions is related to the type of tumour, those types which are most commonly associated with effusion—cancer of the lung, breast, ovary, and gastro-intestinal tract—being the most readily recognized.

The cytological approach to body fluids is of value in demonstrating the presence of suspected cancer and also in gaining information about the origin of a transudate or exudate. It is possible that with the use of cytochemistry the method may become more accurate.

G. Clayton

276. Electron Microscopy and Renal Function in Amyloidosis of the Kidneys

A. BERGSTRAND and H. BUCHT. *Journal of Pathology and Bacteriology [J. Path. Bact.]* 81, 495-503, 1961. 6 figs., 29 refs.

The authors, working at the Karolinska Institute, Sabbatsbergs Sjukhus, and St. Eriks Sjukhus, Stockholm, have examined renal biopsy specimens from 6 patients with clinically moderate to severe renal amyloidosis by electron microscopy as well as light microscopy.

An increased thickening and folding of the basement membrane seemed to be present in most cases and there was no distinct borderline between basement membrane and amyloid. In fact the membrane seemed to disintegrate and disappear in the amyloid mass. The authors conclude that the primary changes in amyloidosis are located in the basement membrane proper of the glomerular capillary wall. The fibrillar structure of amyloid was easily recognized at moderate enlargements and single fibrils of 80 to 100 Å.U. diameter were quite distinct. Such fibrils could not be demonstrated in all amyloid deposits; they did not show the regular pattern of fibrin fibrils, nor did they morphologically resemble collagen or collagen precursors. It is concluded that these fibrils are formed in amyloid and have no relation to fibrin or collagen.

All the patients investigated had signs of a reduced glomerular filtration rate, and in the 3 cases in which catheterization of the renal vein was performed a low filtration fraction was demonstrated. Tubular function, as judged by *para*-aminohippuric acid excretion and the urinary dilution-concentration tests, was less diminished. It is considered that the main cause of the reduced glomerular filtration rate is amyloid deposit on the glomerular basement membrane.

H. Caplan

Microbiology

277. Preliminary Report on a Hemagglutination Test for Entamoebae

J. F. KESSEL, W. P. LEWIS, S. MA, and H. KIM. *Proceedings of the Society for Experimental Biology and Medicine* [Proc. Soc. exp. biol. (N.Y.)] **106**, 409-413, Feb. [received April], 1961. 15 refs.

As previous serological tests for amoebiasis performed with antigens extracted from cultured amoebae grown in symbiosis with bacteria from the intestinal tract have given inconsistent results the authors, working at the University of California, Los Angeles, have employed cultures of *Entamoeba histolytica* and *E. invadens* grown with *Trypanosoma cruzi*, a non-intestinal organism. The antigens were prepared by centrifuging the cultures and removing the trypanosome layer of the sediment. The amoebae were then ruptured and a water-clear extract prepared by further centrifuging. The antigens from the two species of amoeba were compared by means of a modification of the tanned-erythrocyte haemagglutination test, the antibodies employed in this comparison being prepared in rabbits. The experiments showed that there was no cross-reaction between the two species, so that antigen from *E. histolytica* must be used in the study of human amoebiasis.

The sera of patients with amoebiasis were then investigated by the haemagglutination and complement fixation tests. By the haemagglutination technique 61 (98%) of 62 sera from patients with intestinal symptoms or liver abscesses gave a positive reaction, whereas only 1 specimen (2%) of 48 sera from patients not infected with *E. histolytica* did so. A third group of cases consisted of sera from patients infected with *E. histolytica* but without intestinal symptoms; of these, 23 (68%) of 34 gave a positive reaction. Comparison of the results by the haemagglutination test and by the complement fixation technique showed that the antigen could be successfully used in both methods.

R. A. Neal

278. The Fluorescent Antitoxin Test for the Immediate Diagnosis of Diphtheria

J. A. WHITAKER, J. D. NELSON, and C. W. FINK. *Pediatrics* [Pediatrics] **27**, 214-218, Feb., 1961. 7 refs.

The place of the fluorescent antibody technique of staining, which has been used to identify a number of bacteria in smears, in the diagnosis of diphtheria was studied in patients at Parkland Memorial Hospital, Dallas, Texas. As a fluorescent antibody against *Corynebacterium diphtheriae* would probably stain both toxic and non-toxic strains it was decided to try the effect of a fluorescein-conjugated antitoxin rather than an antibody, in the hope that there would be fluorescent staining only of toxin-producing *C. diphtheriae*. The globulin fraction of a potent antitoxin was conjugated with fluorescein isothiocyanate and tested against 15

different pathogenic and non-pathogenic organisms commonly found in the nasopharyngeal or gastro-intestinal tracts. No cross-staining was encountered except for very faint fluorescence of certain types of staphylococci; because of the faintness of the staining and the completely different morphology this caused no difficulty in interpretation. A number of specimens were examined from cases of suspected diphtheria, from patients with proved streptococcal pharyngitis or pertussis, and from a large number of healthy subjects.

The details of the staining technique, which takes one hour, are given. It was observed that toxigenic *C. diphtheriae* had a strikingly characteristic morphology which allowed them to be readily identified. The bright fluorescence formed a halo with no staining of the central part of the organism, presumably owing to the fact that the reaction between antitoxin and toxin occurs on the surface of the organism. When identical fields were examined for fluorescence and by direct illumination it was seen that not all typical diphtheria organisms fluoresced, suggesting that at any one time not all the organisms were producing toxin. Positive slides kept in a refrigerator retained their fluorescent capabilities for about 4 weeks, but at room temperature toxin was destroyed within 48 hours.

No fluorescent *C. diphtheriae* were seen in the throat swabs of 50 healthy children. Similarly, the results of the test were entirely negative in 12 patients with pertussis; however, one of the 10 children with streptococcal tonsillitis did show typical diphtheria organisms, but this patient was not available for further study. The results were also negative in 18 children with non-diphtheritic membranous tonsillitis who were later proved not to have diphtheria, but of 9 patients with proved diphtheria, fluorescent organisms were seen in swab specimens from 8; the smear from the remaining patient was insufficient for adequate examination.

The authors state that healthy carriers of toxigenic *C. diphtheriae* have been detected by fluorescent antitoxin staining. They conclude that this technique should be a useful aid in the rapid diagnosis of diphtheria provided the smears are adequate. It is stressed that a positive result is obtained only with toxigenic strains from proved cases or from carriers and is an indication for antitoxin therapy. A negative smear indicates that the diagnosis must still depend on clinical judgment, culture of the organism, and the results of virulence tests.

R. F. Jennison

279. Method for the Production of a Purified Dry Q Fever Vaccine

S. BERMAN, R. B. GOCHENOUR, G. COLE, J. P. LOWENTHAL, and A. S. BENENSON. *Journal of Bacteriology* [J. Bact.] **81**, 794-799, May, 1961. 10 refs.

Pharmacology and Therapeutics

280. **The Use of Atabrine (Quinacrine) in the Control of Recurrent Neoplastic Effusions: a Preliminary Report**
A. GELLHORN, J. ZAIDENWEBER, J. ULTMANN, and E. HIRSCHBERG. *Diseases of the Chest* [Dis. Chest] 39, 165-176, Feb., 1961. 6 figs., 5 refs.

The value of quinacrine (mepacrine) in the control of neoplastic effusions was studied at the Francis Delafield Hospital, New York, in 21 patients with recurrent pleural effusions secondary to carcinoma of the breast or lung, lymphoma, or mesothelioma and in 10 patients with recurrent ascites secondary to carcinoma of the ovaries, colon, pancreas, or breast or to mesothelioma.

In patients with pleural effusion thoracentesis was performed with removal of about two-thirds of the fluid; this was followed by injection directly into the remaining fluid of 200 mg. of quinacrine dissolved in 10 ml. of sterile water. According to the reaction, 200 to 400 mg. of quinacrine was injected on subsequent days to a total of 1,000 to 2,000 mg. It was usually necessary to repeat the thoracentesis. In patients with ascites sufficient fluid was left after paracentesis to permit ready injection initially of 400 mg. in 20 ml. of water, and then up to 800 mg. depending on reaction, repeated on succeeding days to a total of 3 or 4 g.

Of the 31 patients, 10 were inadequately followed up (9 died within a month) and 5 had additional treatment which invalidated the results. Effective control of the effusion was achieved in 9 patients with pleural and 5 with peritoneal effusion. There was complete failure in one patient in each group. (The authors state that since the paper was submitted for publication complete control has been achieved in 5 additional cases.) Fever, which might last up to 10 days, and regional pain, usually of shorter duration, were the most common toxic reactions. Ileus developed in 2 cases. The authors note that dyspnoea may also occur, due possibly to pleural adhesions or fibrosis, and that caution is therefore necessary in patients with reduced ventilatory capacity. It is emphasized that this treatment will not modify the course of the underlying neoplastic disease.

B. Golberg

281. **The Effects of Synthetic Angiotensin and Noradrenaline on Blood Pressure and Renal Function**
E. G. MCQUEEN and R. B. I. MORRISON. *British Heart Journal* [Brit. Heart J.] 23, 1-6, Jan., 1961. 1 fig., 14 refs.

Angiotensin is a synthetic substance with an extremely powerful vasopressor action. At the University of Otago, Dunedin, New Zealand, the authors have compared the effects of noradrenaline and angiotensin on renal function in 8 male volunteer subjects and its effect on the peripheral veins in 10. The glomerular filtration rate, renal plasma flow, and sodium excretion were determined, using inulin and diodone. The con-

centrations of noradrenaline used were 160 to 320 μ g. per ml. and those of angiotensin 40 to 60 μ g. per ml.; the infusion rate was adjusted to give similar hypertensive responses, noradrenaline being given at a rate of 9.7 μ g. per minute and angiotensin at 1.72 μ g. per minute. The rise in blood pressure which followed infusion was accompanied in each case by a significant diminution in renal function, though this was generally more marked with angiotensin. On the other hand angiotensin had less effect, for example in causing venospasm, than noradrenaline on the peripheral veins. It is suggested that angiotensin deserves further study. G. B. West

282. **Toxic Reactions to Intramuscular Administration of Iron Dextran**

D. BEN-ISHAY. *Lancet* [Lancet] 1, 476-478, March 4, 1961. 19 refs.

At the Rothschild-Hadassah University Hospital, Jerusalem, the author observed 11 cases of severe generalized allergic reaction following administration for hypochromic anaemia of the iron-dextran complex "inferon". In all except one case one or more previous injections of the complex had been well tolerated. There was a history of allergy due to other causes in 3 cases.

The onset of the reaction was abrupt, with fever and a painful swelling of the inguinal lymph nodes. In 8 patients there was tachycardia, while 5 complained of lumbosacral pain and 4 of headache. The leucocyte count was normal in 7 of the 10 patients in whom this was studied and in 3 there was a transient leucocytosis. The erythrocyte sedimentation rate was estimated in 9 cases and found to be increased in all. Electrophoretic examination of the plasma protein pattern revealed an increase in the α_2 - and β -globulin fractions in 5 out of 7 cases. There was no evidence of abscess formation in any of the cases.

The author considers that these toxic reactions render the iron-dextran complex unsuitable for routine use.

Charles Rolland

283. **The Utilization of Iron Administered Orally**

C. W. WOODRUFF. *Pediatrics* [Pediatrics] 27, 194-198, Feb., 1961. 2 figs., 15 refs.

A study of the utilization of orally administered iron in 28 infants aged 7 to 35 months with iron-deficiency anaemia is here reported from Vanderbilt University, Nashville, Tennessee. The fasting patients were given 1 to 3 μ c. of radioactive iron as ferrous sulphate added to a variable amount of a commercial iron compound and the radioactivity in venous blood determined by scintillation counter 7 to 10 days later.

It was shown that the amount of iron utilized for haemoglobin formation did not increase proportionately with an increase in dosage—thus, doubling the amount

of iron administered from 2 mg. per kg. body weight to 4 mg. per kg. made no difference to the amount utilized. The author therefore suggests that single oral doses of ferrous sulphate of the order of 1.5 to 2 mg. per kg. are the most effectively absorbed and he recommends such a dose 3 times daily for a period of 3 months in order to produce a complete cure of iron-deficiency anaemia in infants. In his experience gastro-intestinal disturbances necessitating cessation of the treatment have been infrequent.

A. E. Read

284. Treatment of the Oliguric Patient with a New Sodium-exchange Resin and Sorbitol: a Preliminary Report

R. B. FLINN, J. P. MERRILL, and W. R. WELZANT. *New England Journal of Medicine* [New Engl. J. Med.] 264, 111-115, Jan. 19, 1961. 2 figs., 17 refs.

The administration of exchange resins in the sodium cycle is a recognized means of withdrawing potassium from the patient with oliguria. However, the older resins with a mesh size of over 50 μ were difficult for the patient to take and tended to cause constipation. This paper from Cornell University, New York, describes the use in 10 patients of a sulphonic polystyrene resin of mesh size of 5 to 10 μ which could be taken as a suspension of fine powder. The risk of constipation was met by giving sorbitol in sufficient dosage to produce some looseness of the bowels, 10 to 20 ml. of a 70% syrup being given two-hourly. These measures were effective in lowering the serum potassium level; the use of an osmotic cathartic such as sorbitol also allows some removal of fluid, which is useful in the over-hydrated patient.

[The regimen described recalls the former treatment of intoxication with terra sigillata and purges; but this sophisticated version has more objective evidence in its favour.]

D. A. K. Black

285. Studies of Hepatic Function during Methandienone Therapy

V. WYNN, J. LANDON, and E. KAWERAU. *Lancet* [Lancet] 1, 69-75, Jan. 14, 1961. 1 fig., 22 refs.

Methandienone, a Δ^1 -17- α -methyl testosterone, is an active anabolic agent when given by mouth, with little virilizing effect. It has, like other 17- α -alkyl substituted derivatives of testosterone, a certain effect on liver function, and in the present paper from St. Mary's Hospital, London, a study of this effect is reported. In a group of 30 patients aged 21 to 83 years who received methandienone in a daily dosage of 5 to 100 mg. the serum bilirubin, alkaline-phosphatase, total protein, and glutamic-oxalacetic transaminase (G.O.T.) values were determined, the electrophoretic pattern was studied, and thymol turbidity, flocculation, and "bromsulphalein" retention tests were carried out. None of the patients showed any clinical evidence of liver disease. No abnormal responses were obtained to the older type of liver function test apart from a temporary rise in the serum bilirubin and alkaline-phosphatase levels in one patient. The serum G.O.T. value, however, was raised above the upper limit of the normal in 10 studies on 8

patients and bromsulphalein retention was excessive in 23 patients. Pre-existing liver disease did not increase the incidence of abnormal values for serum G.O.T. and bromsulphalein retention. The authors suggest that administration of the drug should cease if the serum G.O.T. level is persistently raised or exceeds 300 units per ml.

R. Schneider

286. Treatment of Intractable Pain with Morphine and Tetrahydroaminacrine

V. STONE, W. MOON, and F. H. SHAW. *British Medical Journal* [Brit. med. J.] 1, 471-473, Feb. 18, 1961. 13 refs.

Tetrahydroaminacrine (THA) is a partial antagonist to morphine—that is, it antagonizes the depression of the central nervous system caused by morphine without interfering with the pain-relieving effect of the latter. Unlike other partial antagonists THA is a reliable respiratory stimulant and is stable in solution so that it can be dispensed in the same ampoule as morphine. It has been used chiefly in anaesthesia, but a few cases of myasthenia gravis have also been treated with this drug, which is a powerful anticholinesterase.

THA was given in conjunction with morphine to relieve intractable pain in 60 patients with carcinoma at Austin Hospital, Heidelberg, Melbourne, 10 mg. of morphine being administered together with 10 to 15 mg. of THA. If the patient was not completely relieved of pain for 6 hours the dose of morphine was increased until this ideal was reached; 10 to 20 mg. of morphine was usually sufficient in the first instance. As tolerance to morphine or the severity of pain increased so the dose of morphine was increased, but the dose of THA remained the same. No withdrawal symptoms were observed when the dosage of morphine was reduced following palliative treatment. Vomiting occurred in about 1% of cases.

This treatment produced safe, pleasant, and complete analgesia in more than 90% of the cases. There was no problem of addiction, since the patients did not experience euphoria, did not crave for the injections, and suffered no withdrawal symptoms. The side-effects of morphine were reduced; constipation was lessened, pinpoint pupils were not observed, vision was not disturbed, and the patient could cough voluntarily.

It is suggested that a mixture of morphine and tetrahydroaminacrine is excellent for the treatment of patients in their own homes and also for postoperative analgesia.

G. Clayton

287. Measurement of Chronic Pain Relief Utilizing Dose Response of Dextromoramide against Morphine and Placebo

R. O. BAUER, S. M. FREE JR., and E. H. BOWEN JR. *Journal of Pharmacology and Experimental Therapeutics* [J. Pharmacol. exp. Ther.] 131, 373-380, March, 1961. 25 refs.

The authors set out to compare the analgesic effects of dextromoramide with those of morphine and to assess the value of a new method of making such comparisons in patients with chronic pain. At Roswell Park Memorial Institute, Buffalo, New York, 10 patients

suffering from malignant disease and requiring at least 4 doses of potent analgesics a day received a total of 20 courses of injections, each course providing a 5-day regimen of treatment with, respectively, morphine sulphate, a saline placebo, and 2.5 mg., 5 mg., and 10 mg. of dextromoramide. The test injections were given intramuscularly twice a day as required, and a standard analgesic was administered if further relief from pain was needed in any one day. The trial was a double-blind one and the patients were observed hourly throughout.

The data on the duration and "incidence of relief" of pain (defined as more than 50% relief for 1.5 hours) were subjected to analysis of variance. It was found that 10 mg. of morphine sulphate was equivalent in respect of duration of relief to 10.3 mg. of dextromoramide and in respect of incidence of relief to 4.9 mg. of dextromoramide. Euphoria was more frequent with dextromoramide than with morphine, but other side-effects were comparable.

T. B. Begg

288. Pain and the Barbiturates

J. CLUTTON-BROCK. *Anaesthesia* [Anaesthesia] 16, 80-88, Jan., 1961. 6 figs., 6 refs.

In this paper from the University of Bristol the author describes a new method of measuring pain thresholds, in which pressure is applied to the tibia with a modified household spring balance, and application of this method to measurement of the pain threshold following administration of barbiturates.

A group of 12 patients received premedication with morphine or one of its derivatives followed by an intravenous injection of 25 to 100 mg. of thiopentone. In 11 cases in which there was a rise in the pain threshold after premedication the thiopentone reduced the threshold to the premedication level. In other experiments it was found that following prolonged nitrous oxide-oxygen anaesthesia the pain threshold fell very rapidly for the first few minutes and then very much more slowly. Further patients were given 25 mg. of thiopentone during recovery from nitrous oxide-oxygen anaesthesia and a rapid fall in the pain threshold resulted. As the thiopentone became redistributed the threshold rose again and a further dose of thiopentone produced a further fall in the threshold. Similar results were obtained with soluble phenobarbitone, but hydroxydione was found not to have an antanalgesic effect. The clinical implications of the findings are discussed.

Mark Swerdlow

289. The Actions of Amylobarbitone Sodium, Butobarbitone and Quinalbarbitone Sodium upon Insomnia and Nocturnal Restlessness Compared in Psychiatric Patients
J. M. HINTON. *British Journal of Pharmacology and Chemotherapy* [Brit. J. Pharmacol.] 16, 82-89, Feb., 1961. 2 figs., 12 refs.

A controlled double-blind trial is reported of certain barbiturates in the treatment of insomnia in 16 psychiatric patients at the Maudsley Hospital, London, the effect of amylobarbitone, butobarbitone, and quinalbarbitone, each given in doses of 0.1 g. and 0.2 g.,

being compared with that of a placebo. The movements in bed of the patients were recorded by an electronic device, the night nurse estimated sleep or wakefulness every half hour, and the patients' subjective experiences were recorded next morning. All three barbiturates significantly reduced movement in bed and provided less broken and sounder sleep without increased incidence of "hang-over". With a 0.2-g. dose the finer differences between the short-acting and the two intermediate-acting barbiturates in the time of onset and duration of hypnotic action were obscured, whereas a dose of 0.1 g. was insufficient in most cases to produce a significantly different effect from that of the placebo.

I. Ansell

290. A Multivariate Psychopharmacologic Study in Normals

D. R. HAWKINS, R. PACE, B. PASTERNAK, and M. G. SANDIFER JR. *Psychosomatic Medicine* [Psychosom. Med.] 23, 1-17, Jan.-Feb., 1961. 12 figs., 17 refs.

From the University of North Carolina, Chapel Hill, the authors describe a study of four psychotropic drugs in which an attempt was made to assess how far the action of each drug was affected by the following factors: (1) the psycho-physiological make-up of the individual, (2) the chemical properties of the drug, (3) the relationship between subject and experimenter, and (4) the social environment during the experiment. Those taking part were 10 4th-year medical students selected at random who were given by intramuscular injection five preparations, namely, sodium amylobarbitone, 200 mg., chlorpromazine, 25 mg., dextroamphetamine, 10 mg., meprobamate, 200 mg., and normal saline (as a control). The whole experiment consisted of ten 3-hour sessions at each of which each of the test substances was given, using a Latin-square pattern, to 2 of the subjects, so that each subject received each drug twice during the course of the experiment. A psychiatrist and sociologist (themselves unobserved) observed both the subjects and the experimenter during the sessions. A sociometric rating and his score on the Minnesota Multiphasic Personality Inventory were obtained for each subject and at 1, 2, and 3 hours each completed a subjective questionnaire, performed a serial subtraction test, and made a subjective estimate of the effect of the drug.

Analysis of the results showed that chlorpromazine was the most active of the drugs tested, as it proved to be sedating, dysphoric, and caused mental clouding. Amylobarbitone produced less impressive effects, although it also was sedating and caused mental clouding. The action of meprobamate was minimal. Dextroamphetamine produced a slight increase in alertness and promoted a mild euphoria. There was some evidence that the relatively sophisticated subjects used in the study were somewhat inhibited in the experimental situation. However, a more cohesive subgroup among them displayed specially consistent responses and a more accurate perception of subjective changes. It is concluded that this experiment indicates that it is possible to apply quantitative methods to the problem of evaluating the subjective effects of psychotropic drugs.

A. Balfour Sclaire

Chemotherapy

291. *In vitro* Activity of Various Penicillins

C. G. MCCARTHY, G. WALLMARK, and M. FINLAND. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] 241, 143-159, Feb., 1961. 8 figs., 21 refs.

In vitro tests for the susceptibility of 552 strains of 20 species or genera of bacteria were carried out with the following: benzyl penicillin (G), phenoxymethyl penicillin (V), DL-phenoxymethyl penicillin (phenethicillin) and its individual D and L isomers, phenylmercaptomethyl penicillin (PM), synnematin B (SB) and the common nucleus of all of them, 6-aminopenicillanic acid (6APA). The different penicillins varied markedly in their action against the different species and genera, and to a varying extent against strains of the same species. Phenethicillin was more active than V or G against the majority of strains of penicillinase-producing *Staphylococcus aureus*, but the great majority of strains of all other organisms were more susceptible to V and especially to G. The activity of PM closely approximated that of G against most organisms, but the former was more active against many of them. SB was slightly more active against some strains of *Salmonella* and about as active against *Shigella* and *E. coli* as penicillin G, but it was much less active against all other species, particularly those of Gram-positive cocci. Some activity was also exhibited by 6 APA against many of the organisms tested. The importance of considering the antibacterial activity of new penicillins as well as their absorption and other properties, when comparing their therapeutic potentials with those of currently available ones, is thus emphasized.—[Authors' summary.]

292. Effect of Chloramphenicol on Erythropoiesis

P. SAIDI, R. O. WALLERSTEIN, and P. M. AGGELER. *Journal of Laboratory and Clinical Medicine* [J. Lab. clin. Med.] 57, 247-256, Feb., 1961. 8 figs., 21 refs.

Having observed reversible morphological changes in the bone marrow associated with erythroid hypoplasia in patients treated with chloramphenicol the authors studied the effects of this drug on the blood and bone marrow in several clinical conditions.

Of 22 patients given chloramphenicol for various bacterial infections, 10 who had received 40 to 85 mg. per kg. body weight daily for 4 to 27 days showed multiple large vacuoles in the cytoplasm and nuclei of the primitive erythroblasts and this was often associated with a fall in the erythrocyte and reticulocyte counts. The appearances reverted to normal a week after administration of chloramphenicol ceased. No changes were observed in the remaining 12 patients who had received 11 to 45 mg. per kg. daily for 4 to 59 days.

In 4 patients with pernicious anaemia in relapse given chloramphenicol in a dosage of 52 to 60 mg. per kg. daily for 3 to 7 days in addition to vitamin B₁₂ (cyanocobalamin) the marrow, though becoming normoblastic, showed vacuoles in the early erythroblasts. When

chloramphenicol therapy was started 3 days before administration of vitamin B₁₂ the characteristic reticulocyte response was delayed until chloramphenicol had been discontinued; when the latter was given 5 days after the start of vitamin-B₁₂ therapy an initial sub-optimal reticulocyte response was followed by a rapid fall and then by a second peak 8 days after the last dose of chloramphenicol. A similar pattern of events was seen in 2 patients with iron-deficiency anaemia given iron-dextran and chloramphenicol simultaneously. No significant changes in the blood or bone marrow were seen in 7 healthy volunteers given chloramphenicol in a dosage of 44 to 71 mg. per kg. daily for 7 days. It would appear that large dosage and very active erythropoiesis favour the reversible toxic degenerative changes in the early erythroblasts and the depression of reticulocytes which often seems to occur during chloramphenicol therapy.

A. Ackroyd

293. Clinical Evaluation of Cancer Chemotherapy with 5-Fluorouracil

V. K. VAITKEVICIUS, M. J. BRENNAN, V. L. BECKETT, J. E. KELLY, and R. W. TALLEY. *Cancer* [Cancer (Philad.)] 14, 131-152, Jan.-Feb., 1961. 10 figs., 24 refs.

The therapeutic efficacy of 5-fluorouracil in advanced metastatic carcinoma and the factors influencing and methods of preventing toxic effects were studied in 170 patients at the Henry Ford Hospital, Detroit. It was found that the drug was effective only when administered to the point of toxicity. The best results were obtained in cases of carcinoma of the breast, ovary, and bowel and in patients with hepatocellular carcinoma. Confirming the findings of others, the authors state that 5-fluorouracil is not of practical value in the treatment of carcinoma of the stomach.

G. Calcutt

294. Cyclophosphamide in Hodgkin's Disease and Related Disorders

J. Q. MATTHIAS, J. J. MISIEWICZ, and R. BODLEY SCOTT. *British Medical Journal* [Brit. med. J.] 2, 1837-1840, Dec. 24, 1960. 3 figs., 19 refs.

Experience with cyclophosphamide in the treatment of Hodgkin's disease and related disorders is reported from St. Bartholomew's Hospital, London. The 45 patients in the series included 17 with Hodgkin's disease, 3 with lymphosarcoma, 14 with myelomatosis, and 5 with chronic lymphocytic leukaemia. The drug was given intravenously in an initial dosage of 100 mg. daily and then 200 mg. daily to a total of 2 to 4 g. Maintenance doses of 100 to 150 mg. daily were given by mouth. Side-effects were slight, but usually included some depression of the leucocyte count. The drug was found to be particularly effective in Hodgkin's disease (objective improvement being observed in 11 (65%) of the 17 patients), lymphosarcoma, chronic lymphocytic leukaemia, and myelomatosis.

G. Calcutt

Infectious Diseases

295. A Study of the Causes of Diminished Immunity against Diphtheria among Immunized Children. (К изучению причин снижения иммунитета против дифтерии у привитых)

B. E. GRES'-EDEL'MAN, JU. V. ROMAŠKO, A. I. PEDENKO, B. A. KALUŽSKAJA, F. M. ZUNDER, B. S. KRAKOVSKAJA, and R. A. GOL'DENBERG. *Вопросы Охраны Материнства и Детства [Vop. Ohrany Materin. Dets.]* 6, 18-21, Feb., 1961.

In spite of the general immunization of all children against diphtheria in large towns in the U.S.S.R., cases of the disease still occur. The authors therefore performed the Schick test on children between the ages of one and 10 years, the total number tested being 5,605, of whom 712 were attending nurseries, 1,341 a kindergarten school, and 3,552 various other schools. It was found that 18.7% of the total gave a positive result—24.2% of the children in kindergartens, 17.7% of the young school-children, and only 13.1% of those in nurseries. That these results might have been due to incomplete immunization was ruled out (by the finding of only 2 to 10% of incompletely immunized children in the three groups), as was also the effect of the duration of the period since immunization.

The possibility that the diminished immunity might have been due to intercurrent infectious diseases was then investigated. Out of 4,346 fully immunized children, 2,791 (64.2%) had had such diseases. It was shown that of 836 children with a positive Schick test, 770 (92.1%) had had an infectious disease, whereas of those giving a negative Schick reaction, only 50.7% had suffered such an infection. Of all children who had had an infectious disease, 27.5% gave a positive reaction, but of those who had not, only 4.4% did so. The most important infectious diseases were pertussis, measles, tuberculosis, and dysentery, and less important were parotitis, chicken-pox, upper respiratory infections, tonsillitis, epidemic hepatitis, and scarlet fever. It was also shown that there was a definite increase of positive reactions in children who had had several infectious diseases; for example, of those who had had only measles, 30.4% showed a positive reaction, but of those who had had measles and a respiratory infection, more than twice as many (65.8%) did so, the proportion rising with each additional disease.

A further investigation of the 407 children who had actually developed diphtheria revealed that 14.2% were not immunized and 15.5% were not fully immunized. Among the latter cases 89.8% had had at least one infectious disease before the diphtheria occurred, some of them having had several (up to 5). The diminished immunity against diphtheria in fully immunized children was not temporary, nor did it appear only during convalescence from the infectious disease. Thus in children having had infectious diseases it was found that a month

later a positive Schick test reaction was obtained in 34.3% of cases, after 3 months in 31.4%, and after one year in 34.5%. All children with a positive reaction after infectious diseases were given 1 ml. of diphtheria toxoid (anatoxin) and a conversion rate of 95.2% was obtained after 4 to 6 weeks.

H. W. Swann

296. Treatment of the Chronic Alimentary Enteric Carrier

R. G. MAIN. *British Medical Journal [Brit. med. J.]* 1, 328-333, Feb. 4, 1961. 1 fig., bibliography.

The author reviews the treatment of 9 chronic enteric carriers, of whom 8 were faecal excretors of *Salmonella paratyphi B* and the ninth was an intermittent excretor of *S. typhi* and *paratyphi B*; all had been inmates of a mental hospital for several years. One of these patients developed an acute cholecystitis which required surgical intervention (cholecystectomy and choledochostomy), but even after the operation he continued showing positive stools for 4 months; thereafter, however, they became negative and have remained so, even though he returned to his former environment. In view of this result the other 8 carriers were subjected to cholecystectomy, whereupon the stools became negative and repeated investigations of the faeces have continued to show a negative result. All 9 carriers were treated with courses of oral neomycin. Radiological, biochemical, bacteriological, and histological examinations have shown that the gall-bladder and bile-duct are the seat of the persistent infection and that the amount of infection varies with the frequency of excretion. The author reviews the literature of the past 50 years, compares the results of surgical and modern medical treatment, and makes a plea for the wider application of the measures here described for the treatment of chronic carriers of the organisms of enteric disease.

Franz Heimann

VIRAL DISEASES

297. Poliomyelitis Immunization in Infants in the Presence of Maternally Transmitted Antibody

F. T. PERKINS, R. YETTS, and W. GAISFORD. *British Medical Journal [Brit. med. J.]* 1, 404-406, Feb. 11, 1961. 3 figs., 8 refs.

Satisfactory antibody response to poliomyelitis vaccines in infants may be inhibited by maternally transmitted antibodies. The investigation here reported from the University of Manchester and the M.R.C. Biological Standards Control Laboratory, London, was directed towards overcoming this difficulty by increasing the antigenic stimulus. Accordingly, a 3-dose vaccination schedule was instituted for primary immunization of infants in three age groups. As booster, 1 ml. of vaccine was given 12 to 16 months later and serum

antibody titres determined immediately before and 10 to 14 days after this dose.

(1) In 30 infants aged 1 week when primary immunization was started the pre-booster antibody levels for Type-1 virus were generally low. For Type 2, 6 out of 9 infants with high pre-booster titres had been born with low maternal antibody levels and had given a good primary response, while 11 of 13 with low pre-booster titres had been born with high maternal antibody levels and had shown no apparent primary response; similar results were noted for Type-3 virus. Despite the low pre-booster antibody levels, most infants showed a good response to the booster dose, with post-booster titres in some cases rising to 8,192 or higher.

(2) The second group included 40 infants aged 4 months at primary immunization. Those with pre-booster titres of 32 or higher had had non-inhibitory maternal antibody levels and had shown a primary response. Those with pre-booster titres of less than 32 had shown a low or no apparent primary response above maternal antibody levels. Of these infants, all but one (for Type-1 virus) showed good booster responses, post-booster titres being 1,024 or more for Type 2 and 256 or more for Type 3; the majority also showed good titres for Type 1.

(3) The 24 infants in this group were aged 6 to 9 months at primary immunization; maternal antibody had fallen to non-inhibitory levels and all showed a primary response. Few infants therefore had undetectable antibody in the pre-booster sera. In this group booster responses were excellent, all the infants (except 2 for Type-1 virus) showing post-booster titres of 256 or more and the majority titres of 4,000 or more.

The authors stress the importance of a 3-dose schedule for primary immunization of newborn infants. Such increased antigenic stimulus was shown to overcome much of the inhibitory effect of maternal antibody. It is suggested that further improvement might be effected with purified vaccines of higher potency, and this is being investigated. The optimum timing of the booster dose is also discussed.

Joyce Wright

298. Status of Vaccination against Poliomyelitis, with Particular Reference to Oral Vaccination. [Review Article]

J. R. PAUL. *New England Journal of Medicine* [New Engl. J. Med.] 264, 651-658, March 30, 1961. Bibliography.

299. Antibiotics and the Common Cold

C. B. MCKERROW, P. D. OLDHAM, and S. THOMSON. *Lancet* [Lancet] 1, 185-187, Jan. 28, 1961. 5 refs.

The intended purposes of this small trial were "to see if measures to subdue the severity of the common cold prevented exacerbations of bronchitis in subjects with pneumoconiosis" and to determine whether, in normal subjects, treatment could prevent aggravation of the common cold by bacteria normally present in the nasopharynx.

Two groups were investigated during the 7 months preceding the spring of 1959 for the development of colds: (1) 138 men aged 38 to 73 (mean 56.7) years who had pneumoconiosis and bronchitis and were employed in a

light engineering factory in South Wales; and (2) 55 "normal subjects" [undefined] aged 15 to 69 (mean 38) years from the Pneumoconiosis Research Unit of the Medical Research Council at Llandough Hospital, Penarth, Glamorgan. The volunteers were asked to report at the first evidence of a cold. [No criteria given.] Sensitivity tests previously carried out on salivary organisms determined whether tetracycline, oxytetracycline, or chloramphenicol was administered, the dose in each case being 15 mg. 3 times a day for 3 days and dummy lozenges being allocated by random selection in accordance with the "double-blind" principle. In Group 1 50 (36%) of the volunteers reported at least one cold, of whom 8 were excluded from the trial as their salivary organisms were found to be insensitive to all the drugs used. Of the remainder, 23 were treated with active drugs and 19 with dummy tablets. In Group 2 33 (60%) reported colds, 4 being excluded as their salivary organisms were insensitive to the drugs. Of the remainder, 15 received active drugs and 18 dummy tablets. On the hypothesis that the symptoms of a cold are due to the virus for the first few days and that bacteria are responsible thereafter the criterion of successful treatment was the disappearance of the cold by the 4th day.

The results in the individual groups were similar, and only when the groups were combined was a significant effect suggested, 23% being "cured" by dummy lozenges and 50% by active treatment. After the trial the number of subjects whose saliva contained resistant organisms was higher than before; but as the increase occurred about equally among those taking active and those taking dummy lozenges the significance of this finding is uncertain.

[There are a number of variable factors which have to be considered in this trial, and to assess its real value workers in the field are advised to read the original paper.]

K. Schwarz

300. Croup and its Management

J. A. FORBES. *British Medical Journal* [Brit. med. J.] 1, 389-392, Feb. 11, 1961. 11 refs.

The author bases this review of croup and its management upon experience at Fairfield Infectious Diseases Hospital, Melbourne. The diagnostic classification of croup includes laryngeal diphtheria (which remains the prime consideration despite its numerical decline), laryngotracheobronchitis, and "supraglottic oedema" (epiglottitis). It also includes anaphylactoid laryngeal oedema and inhalation of foreign body.

Describing laryngotracheobronchitis, the author lists its progressive stages from the initiating infection of the upper respiratory tract through fever, hoarseness, croupy cough, and inspiratory stridor to increasing obstruction and cyanosis. In 1957 influenza virus was isolated from some cases, while in 1958-9 parainfluenza viruses, Types 1 and 3, were frequently isolated and, more recently, Type 2. Coxsackie virus A 9 was found repeatedly and, less often, E.C.H.O. viruses 14 and 10. From November, 1959, to the end of May, 1960, respiratory viruses were in fact found in 50% of 159 children with croup; in

about 10% of cases there was a primary or secondary bacterial infection, the commonest organisms being *Streptococcus pyogenes* A, staphylococci, and pneumococci. Supraglottic oedema is an acute generalized illness associated with septicaemia. Hoarseness and aphonia are not primary symptoms and the obstructed breathing develops as an expiratory snore. Oedema of the epiglottis and aryepiglottic folds occurs and the progression of obstruction is rapid. During the period 1950-55, when 33 cases were seen, *Haemophilus influenzae* B was isolated from blood cultures in 9 of 19 cases and from the throat or trachea of 24. Less commonly *Str. pyogenes* A may be found.

Because bacterial aggravation of a primary virus infection may be rapid, it is advisable in the treatment of laryngotracheobronchitis to assume that the combined infection is already established. Penicillin, which formed the basis of antibiotic treatment, was given, either alone or with tetracycline in moderately severe staphylococcal or influenzal infections; for more severe infections and for supraglottic oedema chloramphenicol was added, while for diphtheria penicillin was supplemented with erythromycin. Diphtheria antitoxin, as indicated, was given on clinical grounds alone pending the bacteriological results. The patients were nursed in steam-tents. The risks attending the use of oxygen, sedation, and atropine are discussed. The indications for tracheotomy, its site, management, and other matters relating to it are discussed in detail.

Joyce Wright

301. Some Further Virus Isolations from Common Colds D. A. J. TYRRELL and M. L. BYNOE. *British Medical Journal* [Brit. med. J.] 1, 393-397, Feb. 11, 1961. 2 figs., 8 refs.

In continuation of their earlier studies (*Lancet*, 1960, 1, 235 and 237; *Abstr. Wld Med.*, 1960, 28, 95) the authors now report from the M.R.C. Common Cold Research Unit, Salisbury, further isolations of common cold viruses. So far 25 cytopathogenic viruses have been isolated in human embryo kidney tissue cultures from 110 nasal washings and 40 nose or throat swabs collected from persons with colds in the period 1951-9 and in 1960. A further 6 cytopathogenic viruses produced only indefinite changes on passage, while certain other strains, infective to volunteers, were non-cultivable in tissue cultures. The cytopathic changes observed varied from a few slowly developing foci to destruction of the entire culture within a week. The techniques previously described for cultivation of common cold viruses were again used, that is, incubation at 33°C. and with reduced pH, since incubation at 36°C. and the usual pH for conventional tissue cultures resulted in reduction or absence of cytopathic changes.

With one exception washings from which viruses had been isolated, when inoculated nasally into volunteers, produced colds in a varying proportion in each group, as did also 6 of 7 virus strains which had been passaged 4 times in tissue cultures. The viruses could be re-isolated from volunteers with experimental colds; thus following inoculation of 8 different cytopathogenic strains viruses were recovered from 19 of 28 subjects

who developed colds, but from only 3 of 22 who did not. The clinical reactions induced in volunteers were typical of the common cold, although the average clinical picture in any one group appeared to vary according to the virus strain inoculated. Thus there might be differences in degree of constitutional disturbance, amount of nasal secretion, incidence of throat injection, or length of the incubation period.

Serological investigations carried out with rabbit immune sera suggested that the common cold viruses form a heterogeneous group. Strains also appear to vary in their affinity for human or monkey kidney cells in culture. Such heterogeneity may account in part for the frequent occurrence of natural colds in certain individuals; for example, the washings from one subject collected during 4 spontaneous colds in 3 years yielded 3 distinct agents. Marked antibody response to one of these was demonstrable in the natural cold and in an experimental infection with it.

Further investigations will include serological comparison of virus strains, properties of cold viruses, further modification of cultural techniques, use of continuously cultivable cell-lines, and antibody response to infection.

Joyce Wright

302. Inoculation of Human Volunteers with E.C.H.O. Virus Type 20

F. E. BUCKLAND, M. L. BYNOE, L. ROSEN, and D. A. J. TYRRELL. *British Medical Journal* [Brit. med. J.] 1, 397-400, Feb. 11, 1961. 2 figs., 6 refs.

E.C.H.O. virus Type 20 was first isolated in the U.S.A. from children with respiratory tract infection. The present investigation was designed to determine whether intranasal inoculation of this virus type (in throat swab fluid obtained from the National Institutes of Health, Bethesda, Maryland) would infect and induce illness in adult volunteers at the M.R.C. Common Cold Research Unit, Salisbury. Of 8 such volunteers, 5 became infected with the virus and 4 developed an illness. Nasal washings from one of these volunteers were then inoculated into 6 further subjects, all of whom were infected and 5 became ill. A throat swab from the same volunteer was used to initiate serial virus passages in tissue cultures. When the pooled fluids from these were inoculated into 15 volunteers infection developed in 14, 11 of them becoming ill.

Throat swabs and faeces from these subjects were collected on the 1st, 3rd, 5th, and 14th days after inoculation and the presence and, if practicable, the amount of virus in the specimens were determined in tissue cultures. The titres for E.C.H.O. virus Type 20 rose earlier in the throat specimens than in the faeces, but later more virus was found in the faeces than in the throat. In serum samples taken before inoculation and at 14 days thereafter 4-fold (or greater) rises in neutralizing antibody titre against the prototype strain of virus were found in 20 out of 25 paired sera of volunteers from whom virus was recovered. No rises occurred in volunteers from whom virus was not recovered. (Some of the neutralization tests were performed in duplicate at the National Institutes of Health, Bethesda.)

In all, E.C.H.O. 20 virus was recovered from 32 of the 43 volunteers who were inoculated with it and 24 became ill. The incubation period varied from 1 to 5 days. Symptoms included malaise, headache, aching limbs, pyrexia, sore throat, cervical adenitis, and mild alimentary tract disturbances; coryza occurred but rarely. The 11 volunteers who were inoculated with the virus but from whom it was not recovered showed fewer symptoms. In a control group of 33 volunteers inoculated intranasally with uninfected tissue culture fluids, 3 only had symptoms of mild illness.

Joyce Wright

303. Vesicular Stomatitis and Exanthem. A Syndrome Associated with Coxsackie Virus, Type A16

R. L. MAGOFFIN, E. W. JACKSON, and E. H. LENNETTE. *Journal of the American Medical Association [J. Amer. med. Ass.]* 175, 441-445, Feb. 11, 1961. 9 refs.

An epidemic of a syndrome characterized by an acute illness with slight general disturbance and discrete vesicular lesions in the mouth and on the hands and feet occurred in California during the summer of 1959. The first cases were noted in June, and it is estimated that between June and September there were up to 1,000 cases in a population of 500,000. In this paper 33 cases are described together with the results of viral studies in 15 of them.

The first indication of illness was a complaint of soreness of the mouth or refusal to eat. There was little general systemic disturbance, with only a low fever. The most characteristic finding was the presence of a few scattered vesicles or ulcers in the mouth, commonly on the buccal mucosa or tongue. In 8 cases vesicles were also present on the hands, feet, and buttocks. In its typical form the illness was clinically distinguishable from herpangina and the common exanthems; it was highly contagious to other children in the household. Children in the age group 1 to 10 years were chiefly affected (only 6 in this series were over 10 years of age).

Viral studies in 15 cases established that the infection was due to Coxsackie A16 virus in 11.

John Fry

304. Type-3 Adenovirus Infection with Gastrointestinal Symptoms

I. B. R. DUNCAN and J. G. P. HUTCHISON. *Lancet [Lancet]* 1, 530-532, March 11, 1961. 1 fig., 8 refs.

The authors describe from the University of Glasgow the clinical and virological findings in an outbreak of illness which affected 21 members of 5 families in one street in the months of April and May, 1960. The predominant signs and symptoms were diarrhoea, nausea, vomiting, abdominal discomfort, lassitude, and anorexia, which in some cases occurred intermittently. A pharyngoconjunctival-like fever was observed in only 3 cases. The illness was very infectious and the incubation period could have been at the longest only 4 days.

Virological investigations, undertaken on 11 members of two affected families, resulted in the isolation (by thyroid tissue culture) of adenovirus Type 3 from 2 adults and 5 children, the virus being found in 13 of 27 stool specimens, 1 of 3 throat washings, and all of 4 conjunctival swabs. One child aged 6 months was a symp-

tomless faecal excreter, while 4 patients remained faecal carriers after the cessation of symptoms. Virus titres in different faecal specimens varied considerably. The time-relationship between isolation and the appearance of various symptoms in affected persons is shown in a diagram. No bacterial pathogens and no other viruses were detected. One adult from whom Type-3 adenovirus was isolated showed a rise in antibody titres between acute and convalescent phase sera. No adenoviruses were isolated from the stools of 44 control patients with various febrile and neurological disorders.

The human thyroid tissue cultures used for isolation of the virus were examined for up to 21 days for characteristic cytopathic changes, negative specimens being re-tested using HeLa-cell cultures, but no additional virus isolations resulted. Technically, thyroid tissue cultures have the great advantage that no change of culture medium is required during a period of 3 weeks. The authors considered that Type-3 adenovirus was the cause of this outbreak, which, without virological investigations, might have been regarded as "gastric influenza" with unrelated cases of conjunctivitis.

Joyce Wright

305. Vitamin B₁₂ in the Treatment of Botkin's Disease (Infective Hepatitis). (Применение витамина B₁₂ при болезни Боткина)

S. M. BREMENER, R. I. GORDON, L. S. KIRŽNER, D. B. KURAŠEVA, and I. M. RASKIN. *Клиническая Медицина [Klin. Med. (Mosk.)]* 38, 100-106, Dec., 1960. 1 fig., 10 refs.

The authors report a study of 80 patients with infective hepatitis, all of whom were treated with ascorbic acid, 100 mg. daily, intravenous glucose, insulin, and a special diet, while in addition 58 of them received an injection of 30 µg. of vitamin B₁₂ daily for 15 to 20 days, the remaining 22 serving as controls. The experimental group consisted of 48 males and 10 females, of whom over half were under 30 and the great majority under 50 years of age. The disease was mild in 16 cases, moderately severe in 34, and severe in 8.

It was considered that the vitamin had a favourable influence on the main manifestations of the disease. However, the serum bilirubin level remained over 1 mg. per 100 ml. towards the end of the treatment in 18 patients with moderately severe or severe hepatitis. During the disease the vitamin-B₁₂ concentration in the serum was usually increased and that in the liver reduced, while return to normal values coincided with the recovery of liver function. Injections of vitamin B₁₂ seemed to increase the proportion of patients in whom the serum concentration of the vitamin returned to normal. Another effect of the vitamin was to cause a rise in the serum albumin level and a fall in the serum globulin level in a greater proportion of treated patients than in the control group. The authors suggest that, since during the early stage of recovery the hepatic cells seem unable to utilize the vitamin, it is preferably given during the later stages, thereby accelerating complete recovery. They also suggest that determination of the serum vitamin-B₁₂ level can serve as a test of liver function in infective hepatitis.

S. W. Waydenfeld

Tuberculosis

306. Comparative Tuberculin-testing of Human Subjects: a Method of Differentiating the Type of Virulent Mycobacterial Infection

C. J. STEWART, D. P. F. EMBLETON, and D. F. VAN ZWANENBERG. *British Medical Journal [Brit. med. J.]* 1, 7-13, Jan. 7, 1961. 3 figs., 31 refs.

The authors, working at the East Suffolk and Ipswich Chest Service, carried out preliminary tuberculin testing of adults and children with bovine and human P.P.D. in 1957 and in this paper now describe the results of the subsequent testing and relate the findings to the known facts concerning tuberculous disease and infection in each district.

The subjects in the present survey were over 8,000 school-children aged 5 to 18 living in six predominantly rural districts and one group from the City of Norwich. All received two Heaf multiple-puncture tuberculin tests, bovine P.P.D. 1 mg. per ml. (Weybridge) being applied to the right forearm and human P.P.D. 2 mg. per ml. to the left forearm; the depth of puncture was 1 mm. It was found that the results in different districts varied remarkably. Thus in districts with a high incidence of non-pulmonary tuberculosis more children gave a reaction to bovine than to human P.P.D., whereas in districts with a low incidence of non-pulmonary tuberculosis the opposite was the case. In addition, the mean size of the reactions followed the relative incidence of the two forms of tuberculosis.

It is concluded that when school populations are simultaneously tested with human and bovine P.P.D. by means of the Heaf technique there are varying patterns of reactions to the two tuberculins in different districts. There appears to be a qualitative difference in the two types of P.P.D. which can be related to the known history of milk-borne infection in the district and the incidence of pulmonary and non-pulmonary tuberculosis respectively. It is suggested that comparative tuberculin testing can in certain conditions indicate the type of mycobacterial infection. In discussion, the limitations of our knowledge of the materials and technique of comparative tuberculin testing are interestingly reviewed.

Norman F. Smith

307. A Modified Heaf Test Using Old Tuberculin Diluted One in Fifteen

D. H. SHENNAN. *Tubercle [Tubercle (Lond.)]* 42, 33-39, Feb., 1961. 1 fig., 17 refs.

In his work at the Mpilo Chest Unit, Bulawayo, S. Rhodesia, the author used different strengths of old tuberculin (O.T.), decreasing from pure to 1 in 100, for the comparison of the Heaf test with the Mantoux method with 5 units. He came to the conclusion that a dilution of O.T. of 1 in 15 appears to be the nearest equivalent to the Mantoux test. In examining nearly 2,000 African school-children ranging in age from 6 to 18 years simultaneously with the Heaf test as against

the Mantoux test and using two different types of apparatus he was able to show that the Allen and Hanbury tester revealed 0.5% more positive cases than the Mantoux test, while the East machine was less sensitive than the Mantoux test in 8%. The author recommends for selection for B.C.G. vaccination the use of the Heaf test with O.T. in a dilution of 1 in 15 or P.P.D. in equivalent dilution.

Franz Heimann

308. Hydrocortisone Applied Locally to Mantoux Reactions

C. P. SILVER. *Tubercle [Tubercle (Lond.)]* 42, 40-42, Feb., 1961. 7 refs.

The author describes a trial of hydrocortisone carried out at the London Chest Hospital on patients suffering from active pulmonary tuberculosis in whom, following Mantoux testing with 10 units or 1 unit of tuberculin the positive reactions were treated percutaneously with different strengths of hydrocortisone ointment. It was found that the local application of either 1% hydrocortisone ointment or 1% or 2½% hydrocortisone cream 24 or 48 hours after Mantoux testing had no effect upon the diameter of erythema or induration. These negative results are thought to be due to the failure of absorption of hydrocortisone. Control cases treated with the ointment or cream base alone after Mantoux testing showed very little difference in the diameter of erythema and induration.

In a further test the intracutaneous injection into the Mantoux reaction area of either 5 or 7.5 mg. of hydrocortisone sodium succinate 48 hours after the injection of tuberculin sometimes produced a decrease in the erythematous reaction, but no diminution in the induration. The effect of hydrocortisone at this stage of the tuberculin reaction appears to be on the blood vessels rather than on the cellular reaction. The control cases treated with a buffer solution without hydrocortisone showed an initial increase of erythema immediately after the injection, but on the following day the reactions in the hydrocortisone-treated patients and the controls were indistinguishable.

Franz Heimann

309. Clinical Study of the Action of Ethionamide in Association with Other Chemotherapeutic Drugs in the Treatment of Pulmonary Tuberculosis.

(Indagini cliniche sull'azione della tiamide in associazione ad altri chemio-antibiotici nella terapia della tubercolosi polmonare) G. SPINA, M. LUCCHESI, and A. BANCALE. *Rivista della tubercolosi e delle malattie dell'apparato respiratorio [Riv. Tuberc.]* 9, 9-24, Jan.-Feb., 1961. 8 figs., 9 refs.

The authors have treated 39 patients at the Carlo Forlanini Institute, Rome with combinations of ethionamide (1 g. daily) and other antituberculous drugs for several months, 5 receiving ethionamide with isoniazid, 9 with cycloserine, 12 with streptomycin, 4 with kanamycin, 2 with PAS, and 7 with two or more of these drugs.

The results were poor with some combinations, but better with ethionamide in combination with streptomycin (11 becoming sputum-negative on culture) or with cycloserine (8 becoming sputum-negative). There was overall clinical improvement in 29 (74.3%) of the patients, deterioration in 4 (10.2%), disappearance of cavities in 13 patients, and conversion of the sputum to negative in 25 (62.9%). In those patients in whom the sputum remained positive bacterial resistance (growth at concentrations of 5 to 10 $\mu\text{g. per ml.}$) often appeared. The usual symptoms of intolerance to ethionamide were noted in a number of cases.

Arnold Pines

310. Ethionamide (1314Th) in the Treatment of Pulmonary Tuberculosis. Its Possible Place in Relation to Isoniazid in Active Therapy. (L'éthionamide (1314 Th) dans le traitement de la tuberculose pulmonaire. Sa place possible près de l'isoniazide dans la thérapeutique d'attaque)

P. VÉLAN, C. MOIGNETEAU, M. GEFRIAUD, R. TRICHEREAU, and M. CORDIER. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [Bull. Soc. méd. Hôp. Paris] 77, 10-20, Jan. 13, 1961. 20 refs.

The authors report the results of treatment with ethionamide in combination with various other anti-tuberculous drugs in 44 patients with pulmonary tuberculosis which was recent, progressive, cavitated, and often far-advanced. Ethionamide was given in a dosage of 1 g. per day by mouth, sometimes partially replaced or supplemented by suppositories of the drug. Isoniazid was given in a dosage of 8 to 12 mg. per kg. body weight, the duration of treatment ranging from 5 to 18 months.

Of 23 patients given ethionamide and isoniazid, the sputum was negative after 10 months in 22 (95%), while in 17 (73%) radiological resolution was good or very good. Of 21 patients treated with ethionamide, isoniazid, and either streptomycin, PAS, or cycloserine in addition, 20 (95%) became sputum-negative by the 10th month and in 16 (76%) there was good or very good radiological resolution. In another group of 41 patients given ethionamide and [?] daily streptomycin 37 (93%) became sputum-negative and there was good or very good radiological resolution in 24 (60%).

The authors conclude that ethionamide and isoniazid, with or without streptomycin or PAS as well, forms an excellent therapeutic combination [though, as they hint, their study is only suggestive and was not a properly controlled and randomized trial].

Arnold Pines

311. Trial of Aerosols of Kanamycin Combined with Diffusing Agents in the Treatment of Pulmonary Tuberculosis. (Essai de traitement de la tuberculose pulmonaire par des aérosols de kanamycine associée à des facteurs de diffusion)

G. DUMON. *Revue de Tuberculose et de Pneumologie* [Rev. Tuberc. (Paris)] 25, 41-52, Jan. [received April], 1961.

During the past 8 years the author has used aerosols of antibiotics in the treatment of nearly 3,000 tuberculous patients as a supplement to systemic methods of drug administration. The present report is based on the

treatment of 72 tuberculous patients with kanamycin, given as an aerosol with the addition of hyaluronidase. The daily dose of 1 g. was well tolerated [but the duration of treatment is not clearly specified; it appears, however, to have varied from 1 to 3 months in some cases, with longer periods in others]. Some patients complained of the unpleasant odour of the drug, but this was easily disguised by the addition of a few drops of spirit of peppermint.

Patients who had been resistant to neomycin benefited from the kanamycin aerosol in spite of a demonstrated cross-resistance of the two drugs *in vitro*. The effects of the kanamycin aerosol were similar to those obtained with aerosols of streptomycin, isoniazid, or neomycin previously employed by the author. The main indications are in patients resistant to the more usual anti-tuberculous drugs, when kanamycin can be given in combination with cycloserine, neomycin, or ethionamide. In the author's wide experience of this and many other antibiotics the addition of a diffusion factor such as hyaluronidase or thiomucase is essential for success in the aerosol treatment of pulmonary tuberculosis.

A. J. Karlsh

312. The Treatment of Urinary Tuberculosis with 1314 Th [Ethionamide]. (Le 1314 Th en tuberculose urinaire)

— TRUC, — SCHILLIRO, and — DION. *Journal d'urologie médicale et chirurgicale* [J. Urol. méd. chir.] 66, 729-738, Oct.-Nov., 1960 [received Feb., 1961].

From the University of Montpellier the authors report their experience with 1314 Th (ethionamide) in the treatment of 25 cases of renal tuberculosis in patients aged between 20 and 67 years, 16 of them being under 40. In 6 cases the disease was bilateral, in a further 5 it had affected the remaining kidney after removal of the other, and in all cases the disease, which was not recent, had become resistant to the usual combinations of tuberculostatic drugs. The lesions varied between small cavities and large lesions, with or without involvement of the bladder. The drug was given either in the form of tablets (250 mg. each) or of suppositories (500 mg.) in a daily dose of 500 to 1,000 mg. and continued for periods of 40 days at a time for a total of 6 months. The suppositories proved to be more acceptable to some of the patients as nausea, vomiting, diarrhoea, and the unpleasant sensation of a metallic taste in the mouth were common side-effects, necessitating withdrawal of the drug in 7 cases. In addition to ethionamide all the patients received at least one other tuberculostatic drug, in most cases viomycin.

The results were better in the more recent cases; in 8 of 10 patients with a positive urinary culture tubercle bacilli disappeared from the urine, but in 3 reappeared after termination of treatment. In 9 cases the urine was cleared of pus and became sterile, in 5 the urinary findings remained unchanged, and in 4 they became worse. Radiological stabilization occurred in 16 cases, but of 7 severe or long-standing cases, only 2 showed some improvement.

The authors are convinced of the value of the drug and consider that more prolonged studies on a larger number of patients are indicated.

H. F. Reichenfeld

Venereal Diseases

313. **The Discovery of Latent Syphilis in Pregnancy with the Help of the Nelson Test and the Classic Serological Reactions.** (Zur Frage der Aufdeckung latenter Lues der Graviden mit Hilfe des Nelson-Tests und der klassischen serologischen Reaktionen)

M. MEINICKE. *Dermatologische Wochenschrift* [Derm. Wschr.] 142, 1374-1381, Dec. 17, 1960. 28 refs.

In common with recent experience in many countries the number of cases of early syphilis seen at the University Dermatological Clinic, Munich, since 1958 has markedly increased. The author notes that from past experience it can be expected that the incidence of congenital syphilis will also increase in due course. It is therefore now particularly important to test pregnant women for the presence of latent syphilis. At the Munich Clinic 11,153 sera of pregnant women were tested antenatally between 1951 and 1956 by the Meinicke reaction; if the result was positive a number of other standard serological tests, and in special cases the treponemal immobilization (T.P.I.) test, were also performed.

In all, 42 of the women (0.38% of the total tested) were found to be suffering from latent syphilis. In 3 mothers the standard reactions gave a negative result, but the children developed late congenital syphilis; on retesting of those mothers by the T.P.I. test the result was found to be positive. It is suggested that all women with previously treated syphilis should receive penicillin during each subsequent pregnancy, the only exception being patients in whom the response to the T.P.I. test has become negative.

G. W. Csonka

314. **Treponemal Tests in Diagnosis of Syphilis and Biologic False Positive Reactors**

N. J. FIUMARA. *Public Health Reports* [Publ. Hlth Rep. (Wash.)] 75, 1011-1019, Nov., 1960. 5 figs., 10 refs.

The Reiter protein complement fixation (R.P.C.F.) test has been adopted by the Massachusetts Department of Public Health, Boston, as a screening procedure for patients in whom the Hinton test for syphilis has given a positive result. If the R.P.C.F. test also gives a positive reaction the diagnosis of syphilis is held to be confirmed; if negative, a treponemal immobilization (T.P.I.) test is advised. This report describes the results of tests on 703 patients (310 male and 393 female) with persistently positive results by the Hinton test but who presented no clinical, historical, or epidemiological evidence of syphilis. The series consisted of 548 clinic or hospital patients and 155 private patients, and 478 were white and 225 negroes.

Patients were classified as syphilitic if either the T.P.I. or the R.P.C.F. test, or both, were positive, and as biological false positive (B.F.P.) reactors if both the treponemal tests gave a negative result. On this serological evidence 548 patients were judged to have syphilis

and the other 155 were thought to be B.F.P. reactors. It was noted that syphilis was commoner in married or divorced patients of both sexes than in those who were single, in clinic (82.3%) than in private patients (63%), and in coloured (96.4%) than in white patients (69.2%). The infection rate was about the same in the two sexes in each race respectively. Analysis by age showed that in the white patients the incidence of syphilitic reactions increased in frequency from age group 20-24 up to about 45 years of age, after which it tended to level off, but this sharp decrease did not occur in the non-white patients. The greatest incidence of B.F.P. reactions was found in the 15-19 age group, in which 75% of the positive Hinton reactions were classed as non-specific; these were commoner in females.

It is noted that most of the Hinton test results thought to be non-specific were only positive at a low titre ("doubtful" or positive with undiluted serum), the highest titre observed being 1 in 16. It is stressed that reagin tests are still of value in the diagnosis of syphilis since in over 80% of the patients whose sera gave persistently positive results by the Hinton test the diagnosis was confirmed by the response to the more specific treponemal tests.

A. E. Wilkinson

315. **Investigations into the Origin of Toxic-reacting Sera in the Treponemal Immobilization (Nelson) Test. The Effect of Vulcanization Accelerators on *Treponema pallidum*.** (Untersuchungen über die Ursache der toxisch reagierenden Seren im TPI-Test (Nelsontest). Die Wirkung von Vulkanisationsbeschleunigern auf das *Treponema pallidum*)

L. RIETSCHEL and B. ETTIG. *Dermatologische Wochenschrift* [Derm. Wschr.] 143, 241-244, March 11, 1961. 4 refs.

It has previously been found that some rubber stoppers are responsible for test sera becoming toxic and so affecting the results of the treponemal immobilization (T.P.I.) test. In the present study, carried out at the University Skin Clinic, Jena, it was shown that not all rubber stoppers have this effect and that 100% immobilization of the treponemes occurred only in the presence of certain vulcanization accelerators used in the manufacture of some stoppers. Rubber stoppers not containing these accelerators could be used without ill effect on the sera used in the T.P.I. test.

Until rubber which does not contain these harmful chemicals is universally available it is considered advisable to use stoppers made of natural cork.

G. W. Csonka

316. **Syphilis and Serologic Evaluation of Patients: a Recurring Problem**

R. C. DICKENMAN and R. J. KLEINHENZ. *California Medicine* [Calif. Med.] 94, 304-305, May, 1961. 9 refs.

Tropical Medicine

317. Pernicious Anaemia in Jamaica

K. L. STUART and J. E. MACIVER. *British Medical Journal* [Brit. med. J.] 1, 236-239, Jan. 28, 1961. 25 refs.

A study of 10 negro patients admitted to University College Hospital, Jamaica, revealed indubitable diagnostic criteria of pernicious anaemia. All showed a macrocytic anaemia, a megaloblastic bone marrow, and histamine-fast achlorhydria; 7 gave a positive reaction to the Schilling test (excretion of radioactive vitamin B₁₂ (cyanocobalamin) in the urine after administration of radioactive-cobalt-labelled vitamin); and 6 showed the characteristic atrophic gastric lesion. Anorexia, vomiting, and vague abdominal pains were particularly common features; 7 patients showed clinical evidence of peripheral neuritis, 5 also having central cord involvement, and 8 had hepatomegaly and 5 glossitis. All responded satisfactorily to vitamin-B₁₂ therapy.

Previous analyses of hospital admissions have led to the belief that the incidence of pernicious anaemia in negroes is much smaller than in the white races—up to 7 times less frequent. Possible fallacies in these analyses are discussed—such as failure to take into consideration the population density in various age groups and deaths in predisposed individuals before pernicious anaemia is clinically manifest—and the literature on pernicious anaemia in other parts of the tropics is reviewed. It is concluded that while pernicious anaemia occurs more frequently in negroes than has hitherto been thought, dietary and economic factors play a part in this increasing incidence.

The authors suggest that it is recent studies and an increased awareness of allied disorders showing some features of pernicious anaemia that account for an increasing frequency of diagnosis and not a rise in incidence.

Ethel Browning

318. Malignant Lymphoma in African Children. I. A Clinical Syndrome

D. BURKITT and G. T. O'CONOR. *Cancer* [Cancer (Philad.)] 14, 258-269, March-April, 1961. 12 figs., 16 refs.

The authors report the occurrence and describe the features of a clinical syndrome associated with malignant sarcoma of the jaw or abdominal round-cell sarcoma (lymphoma) of identical histology which has been seen with unusual frequency in African children at Mulago Hospital, Kampala, Uganda. More than 120 such cases are now reviewed and the results of a histological study of 106 of them presented. During the 8-year period 1952-9 these tumours constituted 51% of the total incidence of cancer in children recorded at the Kampala Cancer Registry, an incidence in marked contrast to that of 6 to 10% reported for lymphoma in children from other parts of the world. A comparison of the average annual incidence rates per 100,000 children also indicates

that these malignant lymphomata are 4 to 5 times more common in Uganda than elsewhere; leukaemia rates on the other hand are unusually low. Personal inquiry and the replies to a questionnaire have shown that the occurrence of this clinical syndrome in such high incidence appears to be confined to a rather definite geographical area across Central Africa. It is almost entirely concentrated in children between the ages of 3 and 8 years, although 3 cases in patients aged over 14 have been seen. No particular African tribe is especially liable and the series included 2 cases in non-Africans, one of whom was an Indian child and one a European half-caste.

The tumour may present in any one of several anatomical sites and with a variety of clinical manifestations, but there was an absence of significant lymphadenopathy. Of the 106 cases studied, 59 presented with a large and often massive tumour in one or more bones of the jaw, while in addition 8 others had obvious clinical involvement of either the mandible or the maxilla, although this was not the largest tumour present. Loosening of the deciduous molars was often the first symptom, and radiography showed multiple areas of bone absorption and marked displacement of teeth, while displacement rather than invasion was evident in neighbouring tissues. The second most common presenting sign (32 cases) was abdominal swelling. Here the lesions were invariably multiple and involved most structures in the abdomen. Other presenting features were paraplegia from compression of the cord and involvement of the testes, salivary glands, and skeleton other than the jaw by the tumour. In almost all cases two or more of these presenting manifestations were seen in association initially, and more frequently as the disease progressed. Growth of the tumour was extremely rapid and although palliative treatment with nitrogen mustard or more recently with methotrexate produced brief remissions in several cases, most of the children have died in 4 to 6 months. Concurrent manifestations of leukaemia have not been observed in any of the cases.

A. Ackroyd

319. Malignant Lymphoma in African Children. II. A Pathological Entity

G. T. O'CONOR. *Cancer* [Cancer (Philad.)] 14, 270-283, March-April, 1961. 18 figs., 41 refs.

Post-mortem examination of 28 of the 106 cases of malignant lymphoma described above [Abstract 318], 13 affecting primarily the jaw and 15 other sites, revealed that tumour deposits were present in the jaw and other bones (in 54% of cases), the lymph nodes (89%), the liver (54%), kidneys (82%), spleen, adrenal glands (64%), and, in lesser percentages, the stomach and intestines, pancreas, ovaries, testes, the thyroid and salivary glands, and the heart. At all sites the tumour was encephaloid, solid, soft and friable, pale yellow to creamy-white in

colour, and monotonously uniform and homogeneous in appearance. In the larger masses variable amounts of a milky fluid exuded from the cut surface. Necrosis and haemorrhage were present in varying degree depending on the size and location of the lesion and the degree of secondary infection.

In the jaw cases the tumour often involved all 4 quadrants and frequently became confluent in the mandible and maxilla, but rarely fused across the mandibular symphysis. Multiple lesions were found in every jaw case, their distribution pattern being similar to that in the non-jaw cases. Although the adjacent soft tissues were eventually infiltrated, the initial growth was expansive, resulting in compression of surrounding elements and formation of a pseudocapsule. Lymph-node involvement affected especially the retroperitoneal nodes, where massive tumours were frequently the principal cause of the presenting complaint of abdominal swelling. Among the abdominal organs the kidney was most frequently the site of multiple circumscribed lesions, the spleen, surprisingly, being involved in only 11 of the cases coming to necropsy. Involvement of both ovaries was seen in 7 of the 12 females, but testicular involvement in only 3 of the 16 males. Bones other than the jaw were relatively rarely involved, such lesions being demonstrated in only 15 cases (in the femur in 8 and the vertebrae in 7), while lesions of the nervous system were found in only 7 cases.

Microscopically, the lesions showed a surprising cytological uniformity, and the author considers that there is little doubt that these highly malignant tumours take their origin from primitive mesenchymal or stem cells of the reticulo-endothelial system; they were often multicentric. In the entire series of 106 cases histological examination of necropsy or biopsy material showed that the tumour was of the poorly differentiated lymphocytic type in 88, of stem-cell type in 11, of the histiocytic type in 5, and of mixed type in 2. The author concludes that although the disease is undoubtedly neoplastic, the possibility of a priming action on the reticulo-endothelium by some parasite followed by subsequent malignant change must be considered to explain the unusually high incidence and limited geographical distribution throughout central Africa.

A. Ackroyd

320. Portal Hypertension and Gross Splenomegaly in Uganda

H. M. LEATHER. *British Medical Journal* [Brit. med. J.] 1, 15-18, Jan. 7, 1961. 4 figs., 12 refs.

Gross splenomegaly is common in Uganda, but the aetiology is often unknown. Liver disease is also common in Central African natives. All patients admitted to Mulago Hospital, Kampala, Uganda, suffering from gross splenomegaly of unknown origin—47 in all—during a period of about 18 months were therefore studied with the object of determining what relationship, if any, the splenomegaly bore to portal hypertension and liver disease. Leukaemia, active malaria, brucellosis, and schistosomiasis were excluded [but no mention is made of other parasitic infection as a possible aetiological factor].

Of the 45 patients in whom the intrasplenic pressure was measured, this exceeded 25 cm. of water in 24 compared with an average pressure of 16.9 cm. in 18 control subjects without splenomegaly. Liver biopsy was undertaken in 41 cases, and in only 12 of them was a varying but not excessive degree of hepatic fibrosis found, the common lesion (29 cases) being simply a cellular infiltration of the sinusoids and portal tracts. In no case was evidence of extrahepatic portal obstruction discovered, as shown by 19 consecutive investigations by transsplenic portal venography. The author [wisely] points out that similar pathological changes in the liver may be found in African patients with spleens of normal size, and that they have also been reported as occurring in cases of gross splenomegaly in South Arabia and India.

[This paper makes a small contribution to the problem of splenomegaly and portal hypertension in Uganda, but the puzzle of the cause of the splenomegaly still remains unsolved.]

J. W. McNee

321. Experimental and Clinical Studies on Glucocorticoids in Cobra Envenomation

C. BENYAJATI, M. KEOPLUNG, and R. SRIBHIBHADH. *Journal of Tropical Medicine and Hygiene* [J. trop. Med. Hyg.] 64, 46-49, Feb., 1961. 8 refs.

Several workers have reported successful results with glucocorticoids in the treatment of poisoning due to snake bites. The authors of this paper from Chulalongkorn Hospital, Thailand, describe a trial of these compounds in experimental and clinical poisoning due to cobra venom. Preliminary tests showed that dogs given an injection of 2.5 mg. of cobra venom could be protected from almost certain death by administration of 25 mg. of prednisolone succinate 4-hourly until signs and symptoms had subsided. Prednisolone was given intravenously in normal saline and appeared to act up to 4 hours after injection of the venom.

Intravenous injections of 100 mg. of hydrocortisone or 75 mg. of prednisolone succinate were given to 6 patients who had been bitten by a cobra, had received venom antiserum before reaching hospital, and showed serious symptoms of neurotoxic poisoning. All the patients recovered completely without complications. The mechanism of action of the hormone is unknown.

Clement C. Chesterman

322. Energy Requirements of Men in Extreme Heat

C. F. CONSOLAZIO, R. SHAPIRO, J. E. MASTERSON, and P. S. L. MCKINZIE. *Journal of Nutrition* [J. Nutr.] 73, 126-134, Feb., 1961. 21 refs.

From the U.S. Army Nutrition Laboratory, Denver, Colorado, is reported a study which was designed to evaluate the energy requirements of men living and working in extreme heat; it was carried out at Yuma in the Arizona desert, the subjects being 8 healthy young conscientious objectors. The experiment was divided into the three following periods, each lasting 10 days: (1) the men stayed out of doors in direct sunlight from 7 a.m. to 5 p.m. daily; (2) they were again outside but in the shade of a large tarpaulin; (3) they remained indoors in an air-conditioned room. The average daytime tem-

peratures in the 3 periods were 40.5° C. (104.9° F.), 40.3° C. (104.5° F.), and 26° C. (78.8° F.) respectively, while the relative humidity averaged 30.3%, 48%, and 58.5% for the same periods respectively. At night, from 5 p.m. to 7 a.m. next morning, in all periods the men lived in an air-conditioned barracks with a temperature of 26° C. (78.8° F.). An ordinary army diet was supplied ad libitum, except that each item was weighed for each man; only measured soft drinks and an occasional measured drink of beer were allowed after the evening meal. Throughout the experiment the level of daily activity was kept constant, while the energy expenditure was measured by means of indirect calorimetry; the activities measured included walking on the treadmill for one hour on the level at 4 miles per hour, riding the fixed bicycle for 90 minutes, and the various evening activities. The total daily energy expenditure, energy balance, fluid and nitrogen balances, sweat rates, body temperature changes, changes in body weight (5 times a day to the nearest gramme), and urinary and faecal excretion were determined.

The body temperature, the food intake, the energy expenditure in the various resting and exercise activities, and the total daily energy expenditure were significantly higher in Periods 1 and 2 than in Period 3. The gross caloric intake averaged 3,843, 3,778, and 3,394 Cal. and the total energy expenditure 3,517, 3,439, and 3,196 Cal. per man per day for the three periods respectively. The difference was even more significant when the results were corrected for changes in body water and nitrogen balance, making the average energy requirements equivalent to 55.5, 56.4, and 36.6 Cal. per kg. body weight in the three periods respectively. This study therefore showed that there is an increased caloric requirement for men living and working in extreme heat, and the authors suggest that this increase is most probably imposed by "a combination of increased action by the blood in heat transport, increased action of the sweat glands, and increased body temperature", resulting in an increase in the total metabolic rate. They point out that the findings of the present study are contrary to the recommendations of the Food and Agriculture Organization (F.A.O.) of 1957 and of the U.S. National Research Council in 1958 regarding dietary allowances, which were adjusted on the basis of a decrease in caloric intake with an increase in environmental temperature.

Joseph Parness

323. Pure Red-cell Aplasia in Marasmus and Kwashiorkor Treated with Riboflavine

H. FOY, A. KONDI, and L. MACDOUGALL. *British Medical Journal* [Brit. med. J.] 1, 937-941, April 1, 1961. 28 refs.

A feature of kwashiorkor is that in some of the affected children there is increasing anaemia in the recovery phase; this, the present authors have shown, is due to erythrocyte aplasia developing after proper nutritional treatment has begun. Initially, the bone marrow shows normal erythrocyte precursors, but when the anaemia develops hardly any erythroblasts can be found. No single factor has been identified as responsible for this aplasia.

In view of the successful results previously obtained with riboflavine in a case of pure erythrocyte aplasia the authors tried this vitamin in cases of marasmus and kwashiorkor. Of 23 such patients admitted to the children's ward of the King George VI Hospital, Nairobi, 9 showed erythrocyte aplasia and received riboflavine by mouth or by intramuscular injection. There was renewed erythroblast activity in the bone marrow which was followed by a reticulocytosis and a satisfactory rise in the haemoglobin level.

The cause of the syndrome in kwashiorkor is not known, but the authors suggest that the high protein diet which is an essential part of the treatment of this disease may increase the demand for riboflavine beyond available resources.

M. C. G. Israëls

INFECTIOUS DISEASES

324. Preliminary Trial with "Etisul" in Northern Nigeria

D. G. JAMISON, E. PALMER, and R. L. VOLLUM. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [Trans. roy. Soc. trop. Med. Hyg.] 55, 142-148, March, 1961. 19 figs.

For a preliminary trial of "etisul" (ditophal) in the treatment of leprosy at the Sudan Interior Mission Settlement, Katsina, the authors chose 4 patients with advanced lepromatous disease because they had had little previous treatment and many bacilli were present in smears and cellular infiltrate in skin biopsy specimens. Etisul, which is supplied in a tube containing 5 g. of the active principle, was rubbed into the legs and thighs, at first 5 g. twice a week and later 5 g. once a week, for periods of about 2 to 4 months. In addition 25 to 50 mg. of dapsone was given weekly or twice a week. In 2 patients, both of them children, a reaction occurred after a few weeks which necessitated interruption of the treatment.

The number of bacilli observed in skin biopsy specimens diminished greatly during the first two months of treatment and then remained constant; after treatment there was a partial rise in the number in 3 of the 4 patients. Histological examination of the skin specimens showed: (1) a reduction in the number of bacilli, which also became granular and began to disintegrate; (2) fewer foamy cells; and (3) replacement of the lepromatous infiltrate by fibroblasts and lymphocytes. The clinical condition of the patients also improved.

The authors recommend intensive treatment, etisul being rubbed in all over the body for 3 to 4 months and dapsone given concurrently and subsequently.

F. Hawking

325. II. Hookworm Infection and Anaemia in Mauritius

G. STOTT. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [Trans. roy. Soc. trop. Med. Hyg.] 55, 20-25, Jan., 1961. 2 figs., 8 refs.

Malaria has been almost eradicated from the island of Mauritius, but nevertheless the incidence of anaemia is still very high. A preliminary survey carried out by

Woodruff for the World Health Organization in 1955 showed that the anaemia was hypochromic and microcytic and that hookworm infection was common. The present author has amply confirmed these conclusions in an extensive investigation recently undertaken in Mauritian hospitals, villages, and schools. The incidence of hookworm infection was highest in the parts of the island with a heavy rainfall, and the distribution of anaemia paralleled that of the hookworm. Of 284 anaemic patients, 88% had hookworms; the average hookworm load, counted before expulsion by tetrachloroethylene, was 84 worms per person, the highest individual count being 944. There was, however, no significant correlation between the hookworm load and the degree of anaemia. Infection with roundworm appeared to be distributed uniformly throughout the island.

As stated, the anaemia was almost entirely hypochromic and microcytic and was often very severe, some patients having a haemoglobin level of only 1.3 g. per 100 ml. Inquiry showed that the dietary intake of iron was very low and was made lower by the habit of throwing away water in which the daily rice was cooked. In a survey of 297 people in one village the calculated individual intake of iron was 6.3 mg. per day, an amount barely sufficient for normal physiological needs and one which could be completely offset by the losses caused by a load of about 50 hookworms.

The administration of 0.2 g. of ferrous sulphate daily in schools greatly improved the mean haemoglobin levels, and a dose of 6.6 to 10 mg. of iron daily as ferrous sulphate was sufficient to produce significant increases. The administration of anthelmintics, folic acid, or dried skim milk was ineffective alone. The author [very sensibly] recommends that the national diet should be enriched with 10 mg. of iron per head per day and that ferrous sulphate should be given free to pregnant and lactating women. In the clinical management of anaemic patients an anthelmintic should be given in addition to iron therapy in order to reduce the hookworm load and diminish the likelihood of relapse.

L. G. Goodwin

326. Blood Loss from Hookworm Infection

P. W. G. TASKER. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [Trans. roy. Soc. trop. Med. Hyg.] 55, 36-39, Jan., 1961. 2 figs., 15 refs.

In this study of 29 adult patients with *Necator* infections and anaemia, reported from the Institute for Medical Research, Kuala Lumpur, Malaya, the erythrocytes from 20 ml. of blood of 23 of the patients were incubated with ^{51}Cr -labelled sodium chromate and reinjected intravenously, while in the remaining 6 the chromium-labelled cells were introduced into the stomach through a Ryle's tube. Blood and stools were collected and the daily blood loss assessed for 10 to 15 days. One, two, or three doses of tetrachloroethylene were then given to remove all the worms, which were collected and counted. The residual blood loss was determined.

Little reabsorption, usually less than 15%, occurred when the blood was given by stomach tube. The daily

blood loss attributable to the hookworm infection was proportional to the number of worms; thus one patient with a light infection of about 20 worms lost 2 ml. of blood daily, whereas another with a load of more than 1,500 worms lost 90 ml. daily. With increasing worm loads the relative blood loss decreased from about 0.1 ml. per worm per day to about 0.03 ml. per worm per day. The daily blood loss was unrelated to the haemoglobin level and was unaffected by parenteral iron therapy. It is pointed out that even when reabsorption of iron is taken into account, a light infection of 100 worms would represent a daily loss of some 4 mg. of iron, which on a marginal dietary iron intake could result in a negative iron balance. The author concludes: "undoubtedly, the blood-letting powers of the hookworm must be regarded with respect".

[The author died in Malaya before this paper was published. His valuable contributions to research, reported in an admirably condensed and characteristic style, will be greatly missed.] L. G. Goodwin

327. Mass-administration of Diethylcarbamazine Citrate in Preventing Transmission of Aperiodic Human Filariasis G. F. BURNETT and J. U. MATAIKA. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [Trans. roy. Soc. trop. Med. Hyg.] 55, 178-187, March, 1961. 1 fig., 7 refs.

Mass administration of diethylcarbamazine was tried in Fiji in 1957-9 in an attempt to prevent transmission of aperiodic filariasis. The drug was given in a dosage of 400 mg. per adult weighing 60 to 67 kg. once a week for 6 weeks, with proportional doses for children. This course was accepted willingly and completed by 1,226 out of 1,303 subjects. A second course given 6 months later was received with more indifference. The usual minor allergic and toxic reactions occurred in about 20% of the microfilaria carriers, but they seem to have been unimportant and to have had no adverse effects on the acceptability of the treatment. Before treatment 12.2% of the subjects had microfilariae of *Wuchereria bancrofti* in the blood; 4 months after the first course microfilariae were present in the blood of only 6.7% and 4 months after the second course in only 2.7%. The number of microfilariae was also greatly reduced, so that after the second course the count in the population was only 0.8% of its original level. Before treatment 8 out of 1,208 *Aedes* mosquitoes (0.66%) showed mature infective larvae; after the second treatment 832 mosquitoes showed no infective larvae and only a single immature one.

It is considered that this procedure for controlling filariasis would be successful in any area in Fiji.

F. Hawking

328. O'nyong-nyong Fever: an Epidemic Virus Disease in East Africa. II. Isolation and Some Properties of the Virus

M. C. WILLIAMS and J. P. WOODALL. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [Trans. roy. Soc. trop. Med. Hyg.] 55, 135-141, March 1961. 1 fig., 8 refs.

Allergy

329. **Effect of Rubeola, Rubella, Varicella, and a Viral Upper Respiratory Infection upon the Severity of Childhood Asthma: with a Note on the Role of Corticosteroids** C. J. FALLIERS, S. G. HALBERSTEIN, and S. C. BUKANTZ. *Journal of Allergy* [J. Allergy] 32, 69-81, Jan.-Feb., 1961. 5 figs., 19 refs.

The changes produced by intercurrent infectious disease on the course of chronic bronchial asthma were observed at the Jewish National Home for Asthmatic Children, Denver, Colorado, in 15 children with rubeola, 37 with rubella, 17 with varicella, and 99 with an acute influenza-like infection. Of the children with skin rashes who had acute wheezing at the time of their illness, about one-third became free of asthma while the rash was present and for some time after, and a similar improvement occurred in those with upper respiratory viral infection. It was noted that those children who were receiving maintenance doses of steroids for their asthma also responded in a similar way to these infections, and it is concluded that the anti-inflammatory action of steroids does not necessarily alter the course or mask the symptoms of an acute infection. *H. Herxheimer*

330. **Follow-up of Asthmatic School Leavers** R. PROTHERO. *Medical Officer* [Med. Offr] 105, 88-91, Feb. 17, 1961.

A follow-up questionnaire was sent, several years after leaving school, to 50 severe asthmatics who had been under supervision at an asthma clinic, and 34 replies were received. The answers show that the majority are free from attacks, are engaging freely in various occupations and sports and are leading normal lives. Those who still have attacks are able to manage these without medical attention. All had active treatment at the clinic for years and many had been to special schools. The results of the questionnaire raise the question of the degree of natural abatement of childhood asthma to be expected in adolescence and of the extent to which treatment and protection during school life is advisable or necessary. Further follow-up studies are needed.—[Author's summary.]

331. **Bronchial Sensitivity Testing in Asthma: an Assessment of the Effect of Hyposensitization in House-dust and Pollen-sensitive Asthmatic Subjects** M. K. McALLEN. *Thorax* [Thorax] 16, 30-35, March, 1961. 1 fig., 11 refs.

The results of hyposensitization by injection were compared with those of hyposensitization by inhalation in 100 patients attending the Asthma Clinic at University College Hospital, London, 60 of whom were sensitive to house dust and 40 to pollen. Bronchial tolerance of each patient was first established by inhalation of dust or pollen extract in a closed-circuit apparatus. The patients were divided into five groups. Groups 1 and

4 were given, respectively, repeated subcutaneous injections of house-dust extract and grass-pollen extract to a final dose of 1 mg. of house dust or 5,000 Noon units of pollen, the course lasting 12 weeks. In Groups 2 and 5 treatment was with repeated inhalation of aerosolized allergen from the same apparatus as that used for bronchial testing; the duration of inhalation was increased by 30% on successive occasions until the respective solutions could be tolerated for 200 seconds. Group 3 were treated in the same way as Groups 2 and 5, except that saline solutions only were used instead of house-dust extract. The initial bronchial tolerance was identical in the three groups of dust-sensitive patients and the two pollen-sensitive groups.

The response to treatment was assessed by re-exposure to inhalations of dust or pollen. Both pollen-sensitive groups showed a roughly equivalent increase in tolerance, irrespective of the method of treatment. In the dust-sensitive groups, however, there were significant differences—patients treated by inhalation showing greater tolerance than those given injections. The latter were, however, more tolerant than the control group, but the figures were not statistically significant. In 4 of the controls there was an improvement in bronchial tolerance. Tests carried out 6 months after the end of treatment showed that only 30% of the patients retained the increased tolerance and that in the majority tolerance had reverted to the pre-treatment level.

It is pointed out that although there was no clear evidence of increased tolerance to dust following a course of desensitizing injections, it is possible that the use of a more potent dust extract or continuation of the treatment with larger doses would have achieved more definite improvement. *R. S. Bruce Pearson*

332. **A Comparison of the Immunologic and Physiologic Responses of Normal and Allergic Individuals** S. LESKOWITZ and F. C. LOWELL. *Journal of Allergy* [J. Allergy] 32, 152-161, March-April, 1961. 12 refs.

At Massachusetts General Hospital, Boston, the antigens dextran (1 mg. intradermally) and Type-VII pneumococcal polysaccharide (80 μ g. subcutaneously) were given to 30 normal subjects and 27 allergic patients. Before the injection and again 3 weeks after it all subjects were skin-tested with the above substances and also with serotonin, histamine, and the histamine releaser "Compound 48/80". Scratch tests with 6 different inhalant allergens (mostly pollen extracts) were also carried out, and the amount of antibody formed after 3 weeks was determined. There was no difference between the two groups of subjects with regard to their skin reaction to dextran, the pneumococcal polysaccharide, histamine, serotonin, or Compound 48/80, while the production of precipitating antibody was also comparable in the two groups. *H. Herxheimer*

Nutrition and Metabolism

333. **A Case of Kwashiorkor in a 15-Months Old Child.** (Případ kwashiorkoru u 15 měsíčního dítěte) O. SAXL and M. SKOUPÁ. *Časopis lékařů českých* [Čas. Lék. čes.] 100, 215-218, Feb. 17, 1961. 25 refs.

The authors state that up till now cases of kwashiorkor in Czechoslovakia have been observed only in Slovakia and the case here described is the first diagnosed in Bohemia and Moravia. The patient was a Gypsy child and the ninth in the family. It was breast fed up to the age of 9 months and then weaned, but its mother stated that it did not like mixed food and especially refused milk, meat, and eggs. Its diet consisted mainly of tea and potatoes; the child was losing weight and was irritable and whimpering. Bluish spots appeared on its thighs, buttocks, and back, accompanied by swellings which started in the lower extremities and became pronounced on the face. Examination showed that the child had pharyngitis, bronchitis, and an enlarged liver.

Laboratory investigations revealed a complete absence of free hydrochloric acid in the stomach, normal results in liver function tests, and a blood picture of hypochromic anaemia; the haemoglobin value was 70%, erythrocyte count 3,800,000 per c.mm., lymphocytes 8,100 per c.mm. The serum protein level was typically low, the total protein value being 3.3 g. per 100 ml., albumin 2 g. and globulin 1.3 g. per 100 ml.

Treatment with infusions of plasma, increased intake of milk, meat, and eggs, and vitamin C and the vitamin-B complex orally was followed by definite improvement on the 23rd day. The serum total protein level rose to 6.95 g. (albumin 3.6 g. and globulin 3.35 g.) per 100 ml. All the other symptoms disappeared and the child was discharged from hospital on the 42nd day.

Although kwashiorkor is generally considered to be a tropical disease, it may be more frequent in temperate climates than has been supposed, particularly in a mild form which is likely to be overlooked. The effects of antibiotics in this case were very encouraging, tetracycline and aureomycin being especially effective. The mode of beneficial action of these drugs, apart from the support they give to the weakened defence mechanism of the body against secondary infections, is not exactly known.

Paul Frankl

334. **The Influence of Diet on Serum-triglycerides in South African White and Bantu Prisoners**

A. ANTONIS and I. BERSOHN. *Lancet* [Lancet] 1, 3-9, Jan. 7, 1961. 3 figs., 9 refs.

In a previous study (*Lancet*, 1960, 1, 998; *Abstr. Wld Med.*, 1960, 28, 377) the authors showed that patients of both sexes with ischaemic heart disease and also white males over the age of 40 had fasting serum triglyceride levels significantly higher than those in white males under 40, pre-menopausal females, and Bantu males of all ages; in addition the high triglyceride levels were associated

with a greater degree of saturation of the fatty acid components. This further study reported from the South African Institute for Medical Research, Johannesburg, was planned to investigate the influence of short-term and long-term dietary manipulation on the fasting serum triglyceride levels in 25 white and 20 Bantu long-term civil prisoners, ranging in age from 21 to 54 years, the mean ages in the two groups (38 ± 7 and 37 ± 9 respectively) being comparable. None were suffering from manifestations of ischaemic heart disease or other diseases. The food intake was maintained at about 3,000 Cal. a day, the protein content accounting for 15% of this, and throughout the study period normal work was performed by both groups of subjects, no hard labour such as stone-breaking being carried out. The three diets tested were arranged so as to assess the effect of: (1) change from a low-fat, high-carbohydrate diet to a high-fat, low-carbohydrate diet; (2) the replacement of some of the carbohydrate in Diet 1 by different kinds of fats and oils, so as to supply 40% of the daily caloric intake instead of only 15% as before; and (3) change from the high-fat, low-carbohydrate diet back to the low-fat, high-carbohydrate diet, the three diets being maintained for 39, 51, and 32 weeks respectively. All blood specimens were taken in the early morning after an overnight fast and the triglyceride levels estimated in phospholipid-free serum extract by the method of Mendelsohn and Antonis (to be published), the cholesterol ester content determined by the method of Sperry and Webb, and the total serum lipids also estimated.

It was found that when either the white or Bantu subject became habituated to a particular diet the fasting serum triglyceride levels did not differ significantly, and both groups responded in the same way to dietary manipulation. After habituation to the low-fat diet the consumption of a high-fat diet rich in mono-enoic and saturated fatty acids for 51 weeks resulted in a significant rise in the previously low serum triglyceride levels. On changing back from the high-fat to the low-fat diet there was a temporary increase in the triglyceride level, which did not return to base level until after 3 to 6 months. It is suggested that the nature and proportion of the fat may influence the rate of clearance of triglyceride from the blood stream and so affect the fasting triglyceride blood levels.

B. M. Ansell

335. **A Clinical Evaluation of an Anabolic Agent Administered to Underweight Patients in a Gastrointestinal Clinic**

H. BAROWSKY, J. RECHTSCHAFFEN, and S. A. SCHWARTZ. *American Journal of Gastroenterology* [Amer. J. Gastroent.] 35, 37-41, Jan., 1961. 9 refs.

The efficacy of norethandrolone ("nilevar"), a synthetic steroid analogue of testosterone, as an anabolic agent to induce weight gain was evaluated in 25 persist-

ently underweight patients attending a gastro-intestinal clinic. Of these subjects, 10 had gastro-intestinal disease, 12 were diagnosed as having functional dyspepsia, and 3 came to the clinic because they wished to gain weight. After 2 months on a high-caloric diet (3,000 Cal. daily) plus a vitamin-mineral supplement they were then given for a similar period nilevar in a dosage of 10 mg. three times a day. The gain in weight, increase in appetite, and improved sense of well-being were recorded.

The response to nilevar was much more pronounced than to the high-caloric diet. Of the 25 patients, 14 gained between 7 and 15 lb. (3.2 to 6.8 kg.). Eleven of them reported an increase in appetite, and 15 said they had a greater sense of well-being. On the high-caloric diet only 1 had shown a good gain in weight, 2 increase in appetite, and 3 a sense of well-being. It is suggested that nilevar fulfils a definite need in the short-term therapy of the abnormally underweight patient and is most effective in those who have no evident gastro-intestinal pathology.

A. G. Mullins

336. Effect of Dietary Cholesterol upon Serum Lipids in Man

W. E. CONNOR, R. E. HODGES, and R. E. BLEILER. *Journal of Laboratory and Clinical Medicine* [J. Lab. clin. Med.] 57, 331-342, March, 1961. 2 figs., 30 refs.

While the feeding of cholesterol quickly raises the serum cholesterol level in experimental animals, it has been assumed in recent years that the dietary intake of cholesterol in man influences the serum level only very little. In this study 6 middle-aged healthy male prisoners (3 in each group) were alternately kept on a diet containing large amounts of egg-yolk (providing 1,650, 1,900, and 4,800 mg. of cholesterol respectively) and on a cholesterol-free diet. In order to minimize differences in the composition of fats the amounts of saturated, mono-unsaturated, and polyunsaturated fatty acids were similar in the high-cholesterol diet and the cholesterol-free diet.

On the cholesterol-free diet the mean serum cholesterol level declined and on the cholesterol-rich diet the cholesterol level rose substantially in all subjects. The serum phospholipid levels behaved similarly, but the serum triglyceride levels showed less pronounced changes. An increase of the polyunsaturated fatty acid content of the diet with a concomitant decrease in the saturated fatty acids did not lower the serum cholesterol level in patients maintained on the high cholesterol diet. Changes in the dietary protein intake (from 20 to 143 g. per day) had no influence on the serum lipid levels, nor were these altered by a positive or negative nitrogen balance.

Z. A. Leitner

337. The Milk-Alkali Syndrome

R. E. RANDALL JR., M. B. STRAUSS, and W. F. MCNEELY. *Archives of Internal Medicine* [Arch. intern. Med.] 107, 163-181, Feb., 1961. 7 figs., bibliography.

According to Burnett *et al.* (*New Engl. J. Med.*, 1949, 240, 787; *Abstr. Wld Med.*, 1950, 7, 51), who first described the milk-alkali syndrome, its characteristic features are: a history of excessive or prolonged intake

of milk and readily absorbable alkali; a high serum calcium level but without increased urinary excretion of calcium; normal serum phosphate and alkaline-phosphatase levels; renal insufficiency and azotaemia; calcinosis, chiefly band keratopathy; and improvement after restriction of the offending substances. The present authors describe in detail 4 cases which show the possible variations in this syndrome: that hypercalcaemia may persist for months after restriction of the intake of milk and absorbable alkali, that moderate impairment of renal function with nephrocalcinosis may be the only abnormality, and that recognition is possible in the absence of some of the features previously considered to be characteristic.

In 3 of the 4 cases the alkali (calcium carbonate) was not one considered to be readily absorbable. One patient had no hypercalcaemia and 3 had hypercalciuria at some time. Two patients had a reduced serum phosphate level and 2 a raised serum alkaline-phosphatase level. Alkalosis was absent in one case. Only one patient had severe renal insufficiency, and one case was diagnosed only on account of the history, the slight alkalosis, and slight decrease in glomerular filtration rate and concentrating ability, leading to a renal biopsy which revealed nephrocalcinosis. Calcium was present in the periarticular tissues in 3 cases and in the kidneys in both cases in which renal biopsy was performed. Band keratopathy was not present in 2 cases and was transient in a third. Serum calcium and urinary calcium levels increased in 2 cases after the withdrawal of milk and alkali instead of showing the usual change towards normal.

In a detailed discussion on pathogenesis the many deficiencies in knowledge of this syndrome are pointed out. There is definitely an increase in the total body calcium and in the miscible calcium pool, but the absence of a compensating hypercalciuria is surprising and difficult to explain. This might be due to the loss of gastric fluid and its various ions or to the early development of renal failure due to nephrocalcinosis, the result of the large tubular load of calcium and phosphate in the presence of alkaline tubular and peritubular fluids. Overactivity of the parathyroids may play some part. Prolonged positive balances of calcium and phosphate produce oversaturation with these ions and their precipitation in abnormal sites, probably facilitated by the systemic alkalosis.

A. Gordon Beckett

338. Diethylpropion in the Treatment of "Refractory" Obesity

D. A. SEATON, L. J. P. DUNCAN, K. ROSE, and A. M. SCOTT. *British Medical Journal* [Brit. med. J.] 1, 1009-1011; April 8, 1961. 1 fig., 9 refs.

A double-blind trial of diethylpropion ("tenuate") was carried out at the Royal Infirmary, Edinburgh, on 40 out-patients who had been treated for obesity for at least a year but had lost little or no weight. These patients, all women, were divided into 2 equal matched groups, each group receiving 25-mg. tablets of the drug and dummy tablets for alternate periods of 12 weeks. Group I were given the drug for the first period and the

placebo for the second, while for Group II this order was reversed. Each patient took 4 tablets daily, one half an hour before each of the 3 main meals and one late in the evening.

The diethylpropion treatment resulted in a fall in the mean weight of the patients, though this reduction occurred only in the first 8 weeks or so of the 12-week period, the weight generally increasing thereafter. However, the absolute loss of weight was disappointingly small and similar to that previously recorded with the amphetamines and phenmetrazine ("preludin"). No important side-effects were noted. The taking of dummy tablets resulted in an increase in mean weight.

It is suggested that, apart from its expense, diethylpropion seems to be a suitable drug for use as a short-term adjunct to the dietary treatment of obesity.

A. G. Mullins

339. Effective Long Term Weight Reduction: Experiences with "Metrecal"

H. J. ROBERTS. *American Journal of Clinical Nutrition* [Amer. J. clin. Nutr.] 8, 817-832, Nov.-Dec., 1960. 2 figs., 20 refs.

The author discusses the effective management of obesity from the point of view of the general practitioner, with particular reference to the large group of obese patients for whom the usual programme does not suffice. This includes: (1) those with serious and progressive medical disorders to whom prompt weight reduction is mandatory, such as diabetes mellitus, heart disease, arthritis, recurrent thrombophlebitis, peripheral vascular insufficiency, and sciatic neuritis; (2) those requiring elective surgery within the near future, in whom the excessive adipose tissue increases the risk; and (3) those who have become discouraged after a number of futile attempts at weight reduction, with or without medical supervision.

In the experiments reported a "well-conceived" substitute food preparation—"metrecal"—was given to 57 patients selected from the 3 groups mentioned above. Metrecal is stated to represent a blend of food materials providing 900 Calories per $\frac{1}{2}$ lb. (227 g.) of the preparation, the nutrients provided being protein, fat, carbohydrate, ash, and vitamins. It entirely replaces the ordinary diet.

The average total loss of weight during the first week of metrecal therapy was 6.3 lb. (2.858 kg.), with a range of 1 to 12 lb. (0.454 to 5.444 kg.). By the end of the first month the average total loss of weight was 12.8 lb. (5.807 kg.), with a range of 4 to 24 lb. (1.814 to 10.888 kg.). In some cases a diet of metrecal was alternated with a 1,000-Calorie mixed diet. After 6 weeks' therapy there were significant decreases in serum cholesterol level. No deviation in the level of hypoprothrombinaemia ("anticoagulant escape") was observed in 9 patients receiving long-term anticoagulant therapy.

It is suggested that this method of weight control compares favourably with other regimens. It is recommended that the physician should use it as part of a long-term programme, with emphasis on diet, exercise, and an analysis of the more pertinent personality of each patient, together with environmental and psychiatric

aspects. It should never be set forth as a guaranteed method or as a panacea. Only "well-motivated" patients who sincerely wish to lose weight are suitable subjects for the treatment. Those who are being coerced into losing weight might be harmed both psychologically and physically, so that the physician must be certain that the patient is actually in need of vigorous weight reduction. Particular attention is directed to those women with a super-feminine build who in reality are not overweight. It is suggested that such women can be detected by the "pinch" test, which is performed over the lower lateral chest area and produces a deep pinch of less than 1 inch (2.5 cm.) of tissue. It is emphasized that slightly overweight adolescents should not be subjected to intensive weight reduction. Overweight in this age group is usually self-limiting, particularly if the subject comes from an emotionally stable environment. Finally, the patient should understand that close medical supervision is highly important when any weight-reducing diet which contains less than 1,000 Calories a day is taken. Added precautions are necessary with patients suffering from peptic ulcer, gout, diabetes mellitus, or cirrhosis of the liver.

A. G. Mullins

340. Protein-losing Enteropathy in the Sprue Syndrome

R. A. PARKINS. *Lancet* [Lancet] 2, 1366-1369, Dec. 24, 1960. 2 figs., 16 refs.

It has been claimed that serum albumin levels of less than 3.5 g. per 100 ml. are found in 60% of patients with idiopathic steatorrhoea, a finding which has generally been attributed to the malabsorption of protein. An alternative mechanism might be a leakage of protein from the intestine, as described by Gordon (*Lancet*, 1959, 1, 325; *Abstr. Wld Med.*, 1959, 26, 18), a syndrome for which he proposed the name "exudative enteropathy". In the present investigation, carried out at Charing Cross Hospital, London, an attempt was made to correlate serum albumin levels with the absorption or leakage of protein, and also with the degree of steatorrhoea and the histological changes in the intestinal mucosa. Protein absorption was studied by feeding ^{131}I -labelled albumin and protein leakage by the intravenous administration of ^{131}I -labelled polyvinylpyrrolidone, as used by Gordon, the percentage of the administered dose excreted in the faeces being determined in both instances. Biopsy specimens of the jejunal mucosa were obtained by the capsule method of Crosby and Kugler. All three methods are described in detail.

In all, 11 patients with idiopathic steatorrhoea were investigated, including one child with coeliac disease; 7 of these patients had responded to a gluten-free diet. No correlation was found between the serum albumin level and the degree of albumin malabsorption or the degree of polyvinylpyrrolidone leakage in any of these cases. There was also no correlation between the degree of albumin leakage and the severity of the histological changes in the jejunal mucosa. It is concluded that the protein disturbances in sprue are complex and not solely attributable either to protein malabsorption or to increased intestinal permeability, or even to a combination of these two processes.

R. Schneider

Gastroenterology

341. Gastric Biopsy in Patients Suffering from Gastric Dyspepsia. (Gastrobiopsie u nemocných s žaludeční dyspepsií)

M. HRADSKÝ, M. HEROUT, and K. RŮŽIČKA. *Československá gastroenterologie a výživa [Čsl. Gastroent. Výž.]* 15, 143-149, March, 1961. 11 figs., 29 refs.

The authors state that gastric biopsy is a safe method of obtaining information about the histological condition of the mucous membrane of the stomach. They claim that one sample of the mucous membrane represents the state of the whole stomach; when samples have been taken from different parts of the same stomach the histological results have been found identical in 88 to 93% of cases.

The results are herein reported in a series of 61 cases of dyspepsia examined by the authors. In all cases a careful check was first made to exclude a gastric or duodenal ulcer or a tumour. The biopsy was carried out with a biopsy tube of the usual type incorporating certain modifications, which are described and illustrated, the whole procedure being claimed to be simple and safe and to produce no side-effects. A 75-ml. syringe was attached to the tube to provide suction, the tube being introduced after anaesthetization of the nasopharynx. The sample, measuring about 2 mm. in diameter, was fixed in 10% formalin and examined histologically.

In 23 cases (38%) the mucous membrane was normal and in the remaining 38 (62%) it showed the appearances of chronic gastritis. Comparison of the results of gastric biopsy with those of the test meal with histamine showed that the presence of normal gastric acidity does not exclude gastritis. In about 65% of cases hyperacidity was associated with a normal gastric mucous membrane, whereas in about 60% of cases hypoacidity was associated with chronic gastritis.

Paul Frankl

[The method of suction biopsy of the stomach was introduced in 1949 by Wood *et al.* (*Lancet*, 1, 18; *Abstr. Wld Med.*, 1949, 6, 203) and has been widely used since then. In Czechoslovakia, however, as in Russia (see *Abstr. Wld Med.*, 1961, 30, 23), the technique still appears to be something of a novelty.—EDITOR.]

342. Prognosis of the Medically Treated Small Gastric Ulcer. II. Ten-year to Nineteen-year Follow-up Study of 391 Patients

N. E. LARSON, J. C. CAIN, and L. G. BARTHOLOMEW. *New England Journal of Medicine [New Engl. J. Med.]* 264, 330-334, Feb. 16, 1961. 1 fig., 2 refs.

A previous paper (*J. Amer. med. Ass.*, 1952, 150, 781; *Abstr. Wld Med.*, 1953, 13, 289) described the follow-up for 5 to 11 years of 414 patients who received medical therapy for "a small, apparently benign" gastric ulcer at the Mayo Clinic in the period 1940-5. The present paper extends the follow-up period to 10 to 19 years in

respect of 391 of these patients. Medical treatment was instituted with the approval of the consultants in 286 (73.2%) of the 391 cases, but in 74 (18.9%) of them it was instituted because the patient refused surgery and in 31 (7.9%) because of the presence of coexisting disease.

Medical treatment was judged to have been successful in 26.8% (105) of the 391 cases as compared with 20.3% in the earlier follow-up period. In some patients different results were recorded in the 2 follow-up periods: ulcer symptoms recurred in .16 (24.6%) of 65 cases in which medical treatment had previously been regarded as successful, while 47 (41.2%) of 114 patients with persistent ulcer symptoms in the earlier follow-up period now reported complete relief. Medical therapy was abandoned for surgical treatment in 158 cases (40.4%), including 22 (13.9%) with urgent complications of obstruction, haemorrhage, or perforation; the incidence of surgical treatment in the earlier follow-up period was 33.9%. The morbidity of gastric ulcer had persisted in the remainder, consisting of 54 patients living at the time of the later follow-up study and 51 who had died. Of these 51 deaths, 7 were attributed to gastric obstruction, perforation, or haemorrhage and 11 to gastric cancer. The over-all incidence of gastric cancer among the 391 patients was 12.2%; gastric cancer was found in 23.4% of the 158 patients who were ultimately subjected to surgical treatment.

Thus the results of long-term medical treatment of gastric ulcer show a high incidence of recurrences and also of gastric obstruction, perforation, haemorrhage, and cancer.

Joseph Parness

343. Elective Portal Systemic Shunt: an Analysis of 237 Cases

W. V. McDERMOTT JR., H. PALAZZI, G. L. NARDI, and A. MONDET. *New England Journal of Medicine [New Engl. J. Med.]* 264, 419-427, March 2, 1961. 7 figs., 22 refs.

The authors review the results in 237 patients subjected to portal systemic shunt for portal hypertension and/or ascites at the Massachusetts General Hospital, Boston, between 1945 and 1959. Ascites was absent or minimal in 197 of these patients, all of whom had had one or more incidents of haemorrhage, while the operation was performed for intractable ascites in 40 cases. The liver pathology and its underlying cause are stated in all but 4 cases.

Considerable emphasis is placed on the ammonia tolerance test in the diagnosis and selection for operation. A sharp rise in the peripheral blood ammonia level in the first 30 to 60 minutes is considered indicative of spontaneous shunting and therefore of the probable existence of oesophageal varices. A slower rise over

the whole of the 4-hour period of the test is considered indicative of defective synthesis of urea. An absolutely flat curve should rule out the presence of spontaneous shunting, even in the presence of obvious hepatic disease. In selection for operation the following criteria are suggested: (1) good nutritional status without ascites or jaundice and without serious medical contraindications; (2) a serum albumin level over 3 g. per 100 ml. and a bilirubin level less than 2 mg. per 100 ml.; (3) a "bromsulphalein" retention value of less than 25%; and (4) a prothrombin time greater than 50% of normal. If these criteria are rigidly adhered to the mortality of shunt surgery is low. Nevertheless in well over one-third of the cases in this series these optimal conditions did not exist, it being considered that the risk of further haemorrhage was greater than the risk of the operative procedure. Preliminary splenoportography was found to be of great value, especially in the diagnosis of extra-hepatic blocks.

Once the operation has been decided on adequate pre-operative preparation, up to several weeks, in order to improve liver function as much as possible, is necessary. In patients with liver disease the type of anaesthesia is important; in many of the authors' cases hypotensive catheter spinal anaesthesia was used, as well as the more conventional methods. The surgical approach was mostly thoraco-abdominal and a new approach to the portacaval shunt is described. A left thoraco-abdominal approach is used for splenorenal shunts. The mortality in patients undergoing portacaval shunt was 12% and in those subjected to splenorenal shunt it was 17%. The postoperative management is described and the results of studies of the effects of the shunt on portal pressure and hepatic blood flow are reported.

In the 40 cases with intractable ascites treated by a shunt operation there was a high proportion (82%) of successes when a double or side-to-side anastomosis was performed.

The follow-up showed a 5-year survival of 73% in the splenorenal group and one of 65% in the portacaval group, but at 10 years the rate was 43% in both groups. In 22% further bleeding occurred after the shunt, mostly from oesophageal varices, but other causes were peptic ulcer and gastritis; further surgery was required in 6%. Ammonia intoxication occurred in 18%, but in only 8% was it a serious problem necessitating constant medical supervision.

Andrew Desmond

344. Morphine Tolerance in Hepatic Cirrhosis

J. LAIDLAW, A. E. READ, and S. SHERLOCK. *Gastroenterology* [Gastroenterology] 40, 389-396, March, 1961. 4 figs., 21 refs.

Electroencephalogram (EEG) recordings were made in 32 subjects on 36 occasions before administration of 8 mg. or 16 mg. of morphine subcutaneously, and 3 hours thereafter. The method of measuring and grading the EEG response is described.

Eight mg. of morphine produced no EEG change in 7 tests on normal subjects or cirrhotic patients without a history of encephalopathy. In contrast, marked changes were seen in 14 tests on patients with a history of im-

pending or overt hepatic coma; these subjects were often jaundiced and showed ascites. A greater effect was seen with 16 mg. of morphine, but minor changes were also noted in the normal subjects and a dose of 8 mg. produced a better differentiation. The changes induced were the type recorded in spontaneous hepatic precoma. Assessment of the general clinical effect of morphine correlated well but not absolutely with the EEG changes. The EEG effects occurred independently of alterations in arterial ammonium, potassium, or pH levels and in urinary volume and electrolytes. The mechanism of the EEG changes is unknown.

Morphine is contraindicated in patients with liver disease with a history of hepatic encephalopathy or who show jaundice or ascites. It should not be given to patients with liver disease complicated by gastrointestinal bleeding. Morphine (8 mg.) may be useful as a provocative test to assess the liability to develop hepatic coma. This is particularly important in the consideration of candidates for portacaval anastomosis.—[Authors' summary.]

345. Roentgen Examination of the Inferior Vena Cava in Chronic Hepatic Disease. [In English]

O. PETERSEN, N. TYGSTRUP, and K. WINKLER. *Acta radiologica* [Acta radiol. (Stockh.)] 55, 97-102, Feb., 1961. 4 figs., 9 refs.

In this study, reported from Rigshospitalet, Copenhagen, the inferior vena cava was visualized by angiography (using 76% "urografin") in 4 patients with cirrhosis of the liver, one with alcoholic fatty liver, and 5 control subjects with a normal liver. Pressures were recorded from the right atrium and the inferior vena cava below the diaphragm in each case. Narrowing of the vein below the diaphragm was more marked in the patients with liver disease.

[The authors' attempt to express their results quantitatively reveals considerable overlap between the two groups and the degree of narrowing does not correlate well with the transdiaphragmatic pressure gradient.]

P. C. Reynell

346. The Liver and Its Diseases. [Review Article]

H. POPPER and F. SCHAFFNER. *Gastroenterology* [Gastroenterology] 40, 536-552, April, 1961. Bibliography.

347. Primary Carcinoma of the Liver—a Plea for Earlier Diagnosis with Emphasis on the Serum Alkaline Phosphatase Values

L. S. GREENE and L. SCHIFF. *Gastroenterology* [Gastroenterology] 40, 219-223, Feb., 1961. 2 figs., 24 refs.

This report from Cincinnati General Hospital, Ohio, is concerned with the diagnosis of primary carcinoma of the liver. It is pointed out that clinical detection of this condition is difficult, and in fact only 5 of 15 cases seen by the authors in a 2-year period were diagnosed clinically on the basis of onset of abdominal pain or the presence of unexplained weakness and fatigue in a cirrhotic patient.

A large nodular liver is apt to arouse suspicion of metastatic tumour, but secondary deposits are rare in a

cirrhotic liver and a primary hepatic neoplasm is more likely. Estimation of the serum alkaline-phosphatase concentration is thought to be of particular value in the diagnosis of primary hepatoma. The alkaline-phosphatase level is high in this condition, and the authors find a value above 7.2 Bodansky units per 100 ml. (normal 1 to 4 units) affords strong support for this diagnosis. Patients with uncomplicated cirrhosis may have a moderate rise in serum alkaline-phosphatase level, but even jaundiced cirrhotic patients (excluding those with biliary cirrhosis) rarely reach the level of 7.2 units which would have detected in retrospect 64% of 30 patients with primary liver cancer, while including as falsely positive only 2% of patients with uncomplicated cirrhosis.

A. E. Read

348. **Minor Biliary Stasis and its Varieties.** (La cholestase mineure et ses variétés) G. ALBOT and P. DELAVIÈRE. *Semaine des hôpitaux de Paris* [Sem. Hôp. Paris] 36, 3209-3228, Dec. 20, 1960. 14 figs., 35 refs.

In this paper from the Hôtel-Dieu, Paris, the authors discuss the syndrome of cholestasis, which occurs in some patients with incomplete blockage of the common bile duct; such blockage may be the result of postoperative stricture following accidental trauma at operation or of neoplasm, but is most commonly due to stone in the bile duct. They distinguish four main stages in the development of the syndrome which, it is emphasized, can develop in the absence of clinical jaundice, or if this occurs at all it is often quite transitory. The characteristic histological lesion associated with the syndrome is the development in the portal areas of sclerotic changes and the formation of new and prominent bile ductules. Later this lesion may progress to the syndrome associated with secondary biliary cirrhosis. Thrombi in the bile duct are not a feature of this lesion.

Biochemically, there may be little evidence of abnormality, but changes in the serum bilirubin, serum cholesterol, and serum alkaline-phosphatase levels and in "bromsulphalein" excretion are important evidence of its presence. As the clinical and biochemical features are not prominent and radiological visualization of the biliary apparatus is likely to be unsuccessful the authors recommend the early examination of a needle-biopsy specimen of the liver. If the lesion is detected before a biliary cirrhosis develops (as evidenced by abnormal results of biochemical tests, particularly reversal of the albumin:globulin ratio) the situation is still reversible by removing surgically the partial obstruction in the bile duct.

A. E. Read

349. **Jejunal Biopsy in Malabsorptive Disorders of the Adult**

R. H. GIRDWOOD, I. W. DELAMORE, and A. W. WILLIAMS. *British Medical Journal* [Brit. med. J.] 1, 319-323, Feb. 4, 1961. 3 figs., 19 refs.

This paper from the Departments of Medicine and of Pathology, University of Edinburgh, and the Royal Infirmary, Edinburgh, describes the appearances of jejunal mucosa obtained by the peroral biopsy technique

in 24 patients with clinical and laboratory features of "idiopathic steatorrhoea" (primary malabsorptive disease). In addition, 4 patients with steatorrhoea following gastrectomy or gastroenterostomy, one patient with regional enteritis, one with diarrhoea after an ileal resection, and 12 patients with "other medical conditions" were studied. Details of parallel observations on serum levels of vitamin B₁₂ (cyanocobalamin), absorption of ⁵⁸Co-labelled cyanocobalamin, absorption and excretion of folic acid, faecal excretion of fat, glucose absorption, xylose excretion after oral administration, and gastric secretion are reported.

Histological examination of jejunal mucosa revealed 2 types of abnormality: flat mucosal surface (Category 1), in which normal villi are absent, the surface epithelium is abnormal, and the lamina propria shows varying degrees of cellular infiltration; and abnormal villi (Category 2), the villi being abnormally short and broad, with varying degrees of cellular infiltration of the lamina propria but less severe epithelial changes. Normal mucosa is designated Category 3.

Of the 24 patients with primary malabsorptive disease, Category 1, 2, and 3 changes were found in 9, 10, and 5 patients respectively. All of the other 18 patients had normal mucosal appearances. In 4 patients repeat biopsies revealed no change in the histological appearances. One patient showed Category 1 and 2 changes, but the situation here was perhaps complicated by the presence of an ileal carcinoma. There was no obvious correlation between the clinical and laboratory findings and the histological appearances of the mucosa. In particular, diarrhoea was not observed more frequently in patients with Category-1 nor was anaemia commoner in those with Category-2 changes.

It is concluded that peroral jejunal biopsy is a useful procedure in the investigation of patients with malabsorptive disease, but the available evidence does not justify the view that the occurrence of the 2 distinct types of abnormal mucosal pattern necessarily indicates aetiological differences.

Hewett A. Ellis

350. **Intrarectal Treatment of 100 Cases of Ulcerative Colitis with Prednisolone-21-phosphate Enemata**

S. G. F. MATTS. *British Medical Journal* [Brit. med. J.] 1, 165-168, Jan. 21, 1961. 2 figs., 12 refs.

The intrarectal infusion of a solution of prednisolone-21-phosphate has been used at the Royal Hospital, Wolverhampton, for the local treatment of ulcerative colitis for a period of 12 months, and the author now assesses its value. The solution, containing the equivalent of 20 mg. of prednisolone, was dispensed in so-called enema bags for self-medication. Treatment was carried out nightly for an initial period of 28 days, and patients were supplied with reserve bags to be used immediately should a relapse occur. Of the 100 patients who received this treatment, 88 improved, 66 of them having no relapse for 9 months.

No complications are said to have been encountered with this local form of corticosteroid therapy, which is considered to offer advantages over the systemic method of administration.

R. Schneider

Cardiovascular System

351. Electrocardiographic Diagnosis of Left Ventricular Hypertrophy in Hypertension

C. SYMONS and E. WAHL. *British Heart Journal* [Brit. Heart J.] 23, 208-212, March, 1961. 1 fig., 17 refs.

In a study at the Royal Free Hospital, London, various electrocardiographic criteria of left ventricular hypertrophy were related to the degree of hypertension in 333 patients over 40 years of age. Overweight patients and those with other forms of heart disease were excluded. Three grades of hypertension were defined (in mm. Hg): between 160/95 and 190/105, between 190/105 and 220/130, and over 220/130.

In about one-quarter of the patients normal recordings were obtained, though this did not apply to any of the 14 men with the highest grade of hypertension. It is suggested that those with normal electrocardiograms probably correspond to patients with benign hypertension referred to by Evans as "hypertonia". The commonest abnormalities found were, in descending order of frequency, left axis deviation, T inversions in limb leads or V5 and V6, S in V1 deeper than 15 mm., ST depressions in V5 and V6, R in V5 or V6 greater than 26 mm., and the sum of S in V1 + R in V5 or V6 greater than 35 mm. T-wave changes, particularly in men with the highest blood pressures, were taken as evidence of secondary myocardial ischaemia.

J. A. Cosh

352. T Wave Abnormalities in Patients with No Evident Heart Disease: the Effect of Posture

W. M. BONNER and J. R. DURANT. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] 241, 179-191, Feb., 1961. 2 figs., 39 refs.

This study from the U.S. Naval Hospital, Charleston, South Carolina, was undertaken as a result of the finding in 14 patients without heart disease of unexplained abnormalities of the T wave in the electrocardiogram (ECG). The clinical and ECG features of these 14 patients are examined in detail, and as a control the ECGs of 74 patients without any evidence of heart disease were also recorded, twelve standard leads being used and the patients examined in both the recumbent and erect positions.

Of the control group, the ECG showed a normal tracing in 38, flattening of the T wave in 25, and T-wave inversion other than in Lead III in 11; changes in the ECG pattern were more frequently encountered when it was recorded in the erect position. The causes for these orthostatic changes in the T wave are discussed; they were found in most instances to be due to physiological alterations in sympathetic tone. Such a physiological basis can best be determined when extraneous factors are eliminated, that is, when the ECG is recorded under basal conditions somewhat similar to those used in determining the basal metabolic rate. The influence of altered posture, exercise, and hyperventilation can also prove useful in deter-

mining the "innocence" of alterations in the T wave. It is suggested that from a practical standpoint physicians interpreting electrocardiograms should avoid a specific diagnosis when T-wave flattening or inversion alone is encountered and that such changes should be labelled "non-specific", their significance being decided on the basis of the associated clinical features.

P. T. O'Farrell

353. A Hemodynamic Technic for the Detection of Hypertrophic Subaortic Stenosis

E. C. BROCKENBROUGH, E. BRAUNWALD, and A. G. MORROW. *Circulation* [Circulation] 23, 189-194, Feb., 1961. 7 figs., 14 refs.

The authors report the results of haemodynamic studies on (1) 45 patients with acquired aortic valvular stenosis, (2) 30 with congenital aortic stenosis (either valvular, discrete subvalvular, or supra-valvular), and (3) 12 with idiopathic hypertrophic subaortic stenosis. In the first two groups the size of the outflow orifice from the left ventricle is fixed, but in hypertrophic subaortic stenosis the obstruction is due to myocardial contraction and therefore the greater the force of ventricular contraction, the smaller will be the outflow orifice. This fact allows differentiation of Group 3 from the other two groups by a simple haemodynamic test.

Simultaneous left ventricular and arterial pressure recordings were made and particular attention was paid to the heart beats following compensatory pauses after premature beats. In the fixed-orifice cases (Groups 1 and 2) these beats were characterized by higher left ventricular systolic pressures and larger arterial pulse pressures than the normal beats, whereas in the patients with hypertrophic subaortic stenosis the heart beats following premature beats had lower arterial pulse pressures than the normal beats, since the arterial pulse pressure varied inversely with left ventricular systolic pressure and duration of ventricular diastole. The test is based on the fact that the Frank-Starling mechanism (increase of stroke volume following increased diastolic filling) leads to a greater degree of stenosis from more powerful muscular contraction in patients with hypertrophic subaortic stenosis.

K. G. Lowe

354. Indolent *Staphylococcus albus* or *aureus* Bacteremia after Ventriculoatriostomy: Role of Foreign Body in Its Initiation and Perpetuation

R. T. SCHIMKE, P. H. BLACK, V. H. MARK, and M. N. SWARTZ. *New England Journal of Medicine* [New Engl. J. Med.] 264, 264-270, Feb. 9, 1961. 4 figs., 24 refs.

Of 54 patients at the Massachusetts General Hospital, Boston, who underwent ventriculo-atriostomy for the correction of hydrocephalus, 9 developed a *Staphylococcus albus* bacteraemia and 2 a *Staph. aureus* bacteraemia. One of the patients with a *Staph. albus* infec-

tion was also infected with *Alcaligenes faecalis*. A McPherson-type valve sterilized by irradiation was used to make the shunt.

In 4 cases with an indolent *Staph. albus* infection cure was obtained with large doses of penicillin without removing the shunting apparatus; in another 4 cases treatment of *Staph. albus* infection was unsuccessful until the shunt mechanism was removed; in the 2 cases of *Staph. aureus* bacteraemia eradication of the infection was not possible and the patients died.

The authors point out that although normally *Staph. albus* is a harmless saprophyte, in the presence of a foreign body it is capable of producing a chronic indolent infection. They suggest that the organism is introduced at the time of operation.

J. B. Wilson

355. Enterococcal Endocarditis: Report of Nineteen Cases with Long-term Follow-up Data

M. G. KOENIG and D. KAYE. *New England Journal of Medicine* [New Engl. J. Med.] 264, 257-264, Feb. 9, 1961. 13 refs.

The authors have reviewed 19 cases of enterococcal endocarditis treated at the New York Hospital between 1945 and 1959. Three patients died during treatment and of the 16 who were considered to be cured, 10 were still alive more than 5 years after the start of their treatment. The source of the infection was thought to be mainly by way of the genito-urinary tract.

On the basis of their experience the authors recommend that enterococcal endocarditis should be treated by the daily intravenous infusion of 20 million units of aqueous penicillin in 5% glucose or saline solution for 6 weeks. During this time the patient should also have 1 g. of streptomycin intramuscularly every 12 hours for 3 weeks, then 0.5 g. every 12 hours for a further 3 weeks. In spite of this relatively large dose of streptomycin, toxic effects on the 8th nerve were noted in only 2 cases.

J. B. Wilson

CONGENITAL HEART DISEASE

356. Continuous Murmurs in Cyanotic Congenital Heart Disease

M. CAMPBELL and D. C. DEUCHAR. *British Heart Journal* [Brit. Heart J.] 23, 173-193, March, 1961. 11 figs., 23 refs.

A continuous murmur closely resembling that of patent ductus arteriosus may be heard in association with cyanotic congenital heart disease. Of 45 such cases seen at Guy's Hospital, London, 35 had a solitary arterial trunk in place of 2 main vessels leaving the heart (either a persistent truncus or an aorta with pulmonary atresia), and in all the continuous murmur was attributed to the blood flow through the vessels carrying blood to the lungs. In 6 cases this function was performed by a patent ductus and in the remainder by a well-developed system of bronchial or other collateral arteries. The continuous murmur was loud in most patients and was often widely heard on both sides of the chest.

Persistent truncus was proved in only one case, that of a boy who died at 3 years of age in whom bronchial

arteries provided the only route for blood supply to the lungs. In 16 cases the clinical diagnosis of "solitary arterial trunk" was made without its being possible to distinguish between persistent truncus and pulmonary atresia. Of these 16, 9 had pleonaemic lung fields—a surprising finding, as bronchial arteries provided the only source of pulmonary blood flow; the other 7 with oligoemic lung fields were more cyanotic and more disabled, as might be expected. Pulmonary atresia was diagnosed in 18 cases on the basis of operation, angiocardiology, or necropsy, and in all these some elements of the pulmonary arterial system were present. Most patients were considerably disabled. Five had a patent ductus carrying blood from the aorta into the pulmonary system and the remainder had bronchial or other collateral arteries. Fallot's tetralogy was present in 5 cases; 3 had soft continuous murmurs and the other 2 had additional lesions (corrected transposition and situs inversus respectively). Finally, there was a small assorted group of 5 patients with multiple defects, among whom were 3 with absence of the inferior vena cava, venous return from the lower part of the body being via an azygos vein.

J. A. Cosh

357. Anastomosis of the Superior Vena Cava and the Right Pulmonary Artery in the Treatment of Cyanotic Congenital Heart Disease. (L'anastomose veine cave supérieure-artère pulmonaire droite comme traitement des cardiopathies congénitales cyanogènes)

P. SOULIÉ, M. SERVELLE, P. VERNANT, and C. CORNU. *Archives des maladies du cœur et des vaisseaux* [Arch. Mal. Cœur] 54, 1-18, Jan. [received March], 1961. 10 figs., 7 refs.

Direct anastomosis of the superior vena cava to the right pulmonary artery allows the blood from the former to bypass the right side of the heart and any right-to-left shunt and, as in Blalock's operation, adds to the quantity of venous blood entering the lungs but without causing any short-circuiting of blood already arterially oxygenated. Experiments on dogs showed that in spite of the low pressure blood did flow from the vena cava into the pulmonary artery and that sufficient oxygenation was obtained, even with occlusion of the left bronchus.

At the P. Santy Centre for Research in Cardiovascular Surgery, Lyons, this operation has been performed on 13 patients, of whom 9 had Fallot's tetralogy, 2 tricuspid atresia, one Ebstein's disease, and one transposition of the great vessels; 6 of these patients had previously undergone Blalock operations. Two of the patients died, in 2 others there was no improvement, probably because of thrombosis of the anastomosis, but in the remaining 9 there was variable improvement and lessening of the cyanosis. Most patients had temporary engorgement of the face and some developed superficial anastomotic veins. In discussion the authors state that, in theory, this operation might be used for the relief of any malformation where there is an obstruction in the right heart associated with a shunt, but it is not advised when a direct operation would be successful. Thus in cases in which Blalock's operation is appropriate it is to be preferred as being less hazardous. In performing

caval-pulmonary anastomosis, the technique of which is adequately described, complete caval obstruction is avoided by using a lateral clamp, and anticoagulant drugs are given postoperatively. The presence of pulmonary hypertension is a contraindication to the operation.

M. Meredith Brown

358. Congenital Mitral Insufficiency

N. S. TALNER, A. M. STERN, and H. E. SLOAN JR. *Circulation* [Circulation] 23, 339-349, March, 1961. 11 figs., 17 refs.

A brief review of the literature showed that congenital mitral insufficiency is often found in association with other abnormalities, including aneurysmal dilatation of the atrium, reduplication of the mitral orifice, corrected transposition of the great vessels, and patent ductus arteriosus. Though rare, this abnormality may produce severe impairment of cardiac function requiring surgical intervention.

The present authors analyse 10 cases of this condition in patients aged between 9 months and 8 years seen at the University of Michigan Medical Center, Ann Arbor. All the patients had the typical clinical findings of mitral insufficiency. In 7 the diagnosis was confirmed at operation, in 2 at necropsy, and in another by left ventricular angiography. Right heart catheterization was carried out on 8 patients and left heart catheterization by the percutaneous method on 3. On 2 a retrograde left heart catheterization with injection of contrast medium was performed. Three patients had an associated coarctation of the aorta, 2 had corrected transposition of the great vessels, and 2 evidence of a patent ductus arteriosus. Nine of the 10 had had at least one bout of congestive heart failure, while fatigue on exertion, retardation of growth, and frequent respiratory-tract infections were present in all 10. None gave a history suggestive of rheumatic fever. All had some degree of cardiac enlargement, the typical pansystolic murmur of mitral insufficiency, and an apical protodiastolic rumble. Seven had an associated apical thrill. Six cases showed the electrocardiographic (ECG) changes of left ventricular hypertrophy and all showed P mitrale. The ECG changes of right ventricular hypertrophy were found in one case with corrected transposition of the large vessels, and another case with the latter anomaly showed incomplete right bundle-branch block.

The radiological changes consisted primarily in left atrial and left ventricular enlargement. The aorta was characteristically small. In 3 cases the left atrium was aneurysmal in size. Angiography seemed to show that the left atrium was usually much enlarged and formed the right cardiac border, and the right branch of the pulmonary artery was elevated by the enlargement of the atrium. Retrograde left heart catheterization with injection of contrast material into the left ventricle demonstrated regurgitation of contrast material into the left atrium in 2 cases. Right heart catheterization showed pulmonary hypertension in all but one case; in one case it was severe. By left heart catheterization the typical left atrial pressure pulse of mitral insufficiency was obtainable. At necropsy in one case enlargement of the

left atrium and ventricle and a thickened, widely dilated mitral-valve annulus were found; shortened chordae tendineae appeared to restrict valve mobility and there was evidence of endocardial sclerosis. In another case the typical anatomical arrangement of corrected transposition of the great vessels was present and the left atrio-ventricular valve was tricuspid and markedly deformed, with thickened leaflets and shortened chordae tendineae. The left atrium and ventricle were dilated and hypertrophied and several pin-point openings were present in the ventricular septum.

In the 6 cases subjected to operation the mitral insufficiency was corrected by plicating the mitral annulus at one or both commissures with sutures, and in one case by suturing a cleft of the anterior valve leaflet. This resulted in dramatic clinical improvement.

R. Wyburn-Mason

359. Surgical Treatment of Ventricular Septal Defect

J. W. KIRKLIN, D. C. MCGOON, and J. W. DUSHANE. *Journal of Thoracic and Cardiovascular Surgery* [J. thorac. cardiovasc. Surg.] 40, 763-775, Dec., 1960. 2 figs., 20 refs.

An analysis is presented of 320 consecutive cases of ventricular septal defect in which operation was performed at the Mayo Clinic. A low hospital mortality and good results were achieved throughout the 5-year experience in older patients with mild or moderate pulmonary hypertension. Early, the mortality was high among infants and among all patients with severe pulmonary hypertension. Refinements in techniques of perfusion, operation, and management produced markedly improved results in these groups.—[Authors' summary.]

360. Transposition of the Great Vessels: Surgical Palliation during Infancy

A. J. MOSS, J. V. MALONEY JR., and F. H. ADAMS. *Annals of Surgery* [Ann. Surg.] 153, 183-192, Feb., 1961. 5 figs., 23 refs.

The authors, from the University of California Medical Center, Los Angeles, report the results in 6 infants operated on for transposition of the great vessels associated with increased pulmonary blood flow. The technique is as follows. Through a right antero-lateral thoracotomy in the 4th space a large atrial septal defect is created by the Blalock-Hanlon technique (*Surg. Gynec. Obstet.*, 1950, 90, 1; *Abstr. Wld Surg.*, 1950, 8, 62). A pulmonary-caval shunt is also produced by anastomosing the proximal end of the apical segmental branch of the pulmonary artery to the proximal end of the azygos vein. This anastomosis increases the oxygenation of blood in the superior vena cava and therefore in the right atrium, right ventricle, and aorta; it also increases the shunt of blood through the atrial septal defect by causing an imbalance in the pulmonary and systemic circulations. The rationale of the operation is based upon the assumption that in foetal life most of the inferior-caval blood passes through the foramen ovale to the left atrium, while the superior-caval blood passes mainly into the right ventricle. Thus it is hoped that

following the creation of the atrial septal defect the de-saturated inferior-caval blood will pass mainly into the pulmonary artery, while the partially oxygenated superior-caval blood will pass mainly into the right ventricle and aorta.

In the 3 infants who survived the operation there was clinical improvement, with an increase in oxygen saturation of the systemic blood.

R. L. Hurt

361. Endocardial Cushion Defects

I. M. ANDERSON and H. M. T. COLES. *British Medical Journal* [Brit. med. J.] 1, 696-705, March 11, 1961. 22 figs., 17 refs.

In this study the authors adopted the 3-grade classification of endocardial cushion defect proposed by Campbell and Missen (*Brit. Heart J.*, 1957, 19, 403; *Abstr. Wld Med.*, 1957, 22, 446), namely, Grade I representing an ostium primum defect between the two atria with deformity of a cusp of the mitral valve and possibly also of the tricuspid valve; cases of Grade II have an added high ventricular septal defect; while in Grade III there is a common atrio-ventricular canal. They then review 10 cases seen at the Westminster Hospital, London, out of a total of 248 children with congenital heart disease, an incidence of 4% in this highly selected population. The final diagnoses were Grade-I defect in 4 cases, Grade II in 4 (one with patent ductus), and Grade III in 2 (one with patent ductus); only 2 of the patients in the series were mongols. Also described are 2 children with large ostium secundum defects which were diagnostically indistinguishable from the 10 others until the heart was opened at operation.

Of the 10 patients, 9 were seen in the first year of life because of dyspnoea and failure to thrive. They showed cardiac enlargement and usually a loud systolic murmur, maximal to the left of the lower sternum, sometimes with a thrill, suggesting ventricular septal defect; in 5 there was also an apical diastolic murmur. Radiography revealed enlargement of all chambers of the heart with pulmonary plethora, or when pulmonary resistance was high, oligoemia of the peripheral lung fields. The electrocardiogram showed left axis deviation, with hypertrophy of the right ventricle and sometimes of both ventricles. Cardiac catheterization studies confirmed the presence of a shunt into the right atrium in 8 cases and into the right ventricle in 2. Pulmonary arterial pressures ranged up to 83/43 mm. Hg, usually due to a high pulmonary flow; in only one case was there very high pulmonary resistance. Passage of the catheter from the right atrium to the left at a low level suggested that the lower margin of the defect reached the level of the A-V valves. Dye curves showed the same pattern whether the dye was injected into the right or left pulmonary artery, indicating that the interatrial defect was large, so that the shunt of dye across it occurred equally easily whether dye entered the left atrium via the right or the left pulmonary veins. In performing angiocardigraphy injection of the contrast medium was usually made into the outflow tract of the right ventricle and was followed by simultaneous opacification of all four chambers owing to the presence of interatrial and interventricular defects.

Of the 10 patients, 4 died of heart failure, 3 being still under one year of age, and 5 were subjected to open heart surgery (by Drew), of whom 3 recovered and did well. The 10th child underwent operation at 3 months of age for relief of pulmonary hypertension by "banding" of the pulmonary artery, but died of cardiac arrest. The 2 patients with a large ostium secundum defect were also operated on, one recovering. In their summing-up the authors state that initial medical treatment for heart failure in early childhood is commonly necessary, after which corrective surgery should be attempted as soon as practicable. Since it is impossible to distinguish with certainty between a large ostium secundum defect and endocardial cushion defect, the surgeon must in such cases be prepared to deal with both interatrial and interventricular defects.

J. A. Cosh

CORONARY DISEASE AND MYOCARDIAL INFARCTION

362. Angina Pectoris. Treatment with Isosorbide Dinitrate

S. SHAPIRO. *Angiology* [Angiology] 12, 53-56, Feb., 1961. 7 refs.

The author reports a clinical trial of the coronary vasodilator isosorbide dinitrate ("isordil"), an isomer of isomannide dinitrate, in the treatment in private practice of 51 patients suffering from repeated attacks of severe angina pectoris. The drug, which is rapidly absorbed and has a long duration of action, was given in an initial dosage of 20 mg. three times a day, reduced to 10 mg. thrice daily for maintenance therapy. According to the response to treatment the patients could be divided into three categories: (1) in 17 there was notable lessening of the severity and frequency of anginal attacks and eventually almost complete cessation of pain, so that no further nitroglycerin was required; (2) in 22 patients the attacks diminished in severity and frequency, but the occurrence of some painful seizures of mild intensity necessitated the occasional use of trinitrin (nitroglycerin requirement reduced to half or less); (3) the 13 remaining patients derived no benefit from the drug. Thus 39 out of the 51 patients (75%) were improved or greatly improved, a result which, in view of the uniform severity of the condition in these patients, the author considers satisfactory.

A. I. Suchett-Kaye

363. Comparison of Subjective and Objective Assessment of Angina Pectoris

J. R. A. MITCHELL. *British Medical Journal* [Brit. med. J.] 1, 791-792, March 18, 1961. 4 refs.

The study here reported was carried out at the Radcliffe Infirmary, Oxford, in an attempt to find if any correlation existed between subjective and objective assessment of the severity of symptoms in patients with angina pectoris. The study covered 11 patients (10 male and 1 female) with a clear-cut clinical history of angina pectoris who were seen every 3 to 6 months for periods ranging from 6 months to 2½ years. At each visit the patients were asked about frequency and duration of

attacks of pain and the amount of exertion needed to produce pain; they were also asked to say whether they were "improved", "unchanged" or "worse". Each patient then performed a standard exercise test until pain occurred. This was performed at a constant rate, at the same time of day, wearing the same clothes, and after sitting quietly at rest for 15 minutes. The time from the start of the exercise to the onset of pain was carefully recorded, as was also the time taken for the pain to pass off. Eight patients thought they had improved during the period of observation and 3 that they were unchanged or worse. Of the former, only 3 had better performances in the exercise test, the remainder being unchanged or worse. Of the 3 patients who thought they were unchanged or worse, 2 improved their performance in the exercise test.

It is concluded that there are considerable difficulties in using subjective records of improvement to assess the value of any drug in angina pectoris. The use of a carefully standardized exercise tolerance test would overcome some of the difficulties.

C. Bruce Perry

364. Nialamide Treatment of Angina Pectoris: a Double-blind Trial. [In English]

A. LUNDBERG and H. E. SJÖBERG. *Acta medica Scandinavica* [Acta med. scand.] 169, 351-356, March, 1961. 21 refs.

Nialamide, a monoamine oxidase inhibitor akin to iproniazid, was given in 19 established cases of angina pectoris at Södersjukhuset, Stockholm. The drug was administered in 25-mg. doses 4 times daily for 4 weeks (increased to 150 mg. daily for the last 5 days) and a placebo given in similar fashion for 4 weeks either preceding or following the nialamide treatment. The patients and physicians were unaware which treatment was being given at any time during the trial, and only after the trial was the situation disclosed to the patients. No significant variation in frequency or severity of attacks, requirement of trinitrin tablets, blood pressure, or response to exercise was noted throughout, and it was the opinion of the authors that over the relatively short period of the trial nialamide was of no clinical value. Mild degrees of mental irritability occurred in 7 cases during nialamide therapy, but also in 3 during the placebo period.

J. Robertson Sinton

365. Clinical Evaluation of Pheniprazine in Angina Pectoris

G. SANDLER. *British Medical Journal* [Brit. med. J.] 1, 792-794, March 18, 1961. 1 fig., 9 refs.

A clinical trial of a new monoamine oxidase inhibitor, pheniprazine (β -phenylisopropylhydrazine; "cavodil"), was carried out at the Sheffield Region Cardiovascular Centre on 12 out-patients aged 49 to 70 with typical angina pectoris, a double-blind technique being employed. After a control period when only trinitrin was given one month's supply of pheniprazine or of a placebo identical in appearance was provided. Neither patient nor observer knew which drug was given. The dose was two 3-mg. tablets twice daily. A specific number of trinitrin tablets were also given, the number taken being

checked to ensure an objective assessment of the number of attacks of pain. In addition a standardized exercise tolerance test was carried out at monthly intervals and the time taken before the patient was stopped by pain or dyspnoea noted. An electrocardiographic recording was made before and after the exercise.

In 8 cases the administration of both pheniprazine and placebo produced a fall in the consumption of trinitrin. Although the mean weekly consumption of trinitrin over the whole series was less when pheniprazine was being taken than during the control period, the difference was not statistically significant. Neither did the trinitrin requirement during placebo administration differ significantly from the control period or the period of pheniprazine medication. The exercise tests showed an increase with both placebo and pheniprazine, which was significant in the case of the latter. Ischaemic changes were present in the electrocardiogram after exercise in 8 cases during pheniprazine treatment which in 3 cases did not occur during the control period. One patient who stated that he was better and had a better exercise tolerance showed increased electrocardiographic changes after exercise. It appears that the euphoria which may follow administration of pheniprazine may result in greater activity with no corresponding increase in myocardial blood supply, the potential danger of which is pointed out. It is concluded that pheniprazine not only is of no value in the treatment of angina pectoris, but may be contraindicated.

C. Bruce Perry

366. Clinical Assessment of "Etrynit" for Angina Pectoris

E. SOWTON and S. ORAM. *British Medical Journal* [Brit. med. J.] 1, 794-795, March 18, 1961. 4 refs.

"Etrynit", the trinitric acid ester of trimethylol propane, was compared with glyceryl trinitrate for the rapid relief of pain in angina pectoris in 35 patients (20 men and 15 women) attending King's College Hospital, London. Each patient was given 2 boxes, one containing glyceryl trinitrate in tablets of 1/130 gr. (0.5 mg.) and the other 10-mg. tablets of etrynit to be taken sublingually. The boxes were identified by numbers. Each patient was asked to use all the tablets in one box before starting on the other and to report which tablets proved most effective for the relief of pain. Of the 35 patients, 8 were unable to decide between the boxes and 5 refused to complete the trial. Of the remaining 22, 12 preferred glyceryl trinitrate and 10 etrynit. There was an equal incidence of side-effects. It was found, however, that 5 mg. of etrynit was often adequate and that with this dose side-effects were less severe than with 0.5 mg. of glyceryl trinitrate.

It is concluded that etrynit is as effective as glyceryl trinitrate for the acute pain of angina pectoris and is worthy of further study.

C. Bruce Perry

367. Myocardial Infarction among Middle Aged Oslo Males 1956-57

K. WESTLUND and A. HOUGEN. *Journal of the Oslo City Hospitals* [J. Oslo Cy Hosp.] 11, 21-71, Feb., March, April, 1961. 4 figs., 12 refs.

368. The "Comprehensive" Treatment of Myocardial Infarction. (Über die "komplexe" Behandlung des Koronarinfarctes)

R. FAUSTMANN, H. J. ILTGEN, G. SAASE, and K. H. ALBAUM. *Münchener medizinische Wochenschrift* [Münch. med. Wschr.] 103, 242-247, Feb. 3, 1961. 2 figs., bibliography.

In the period 1948-55 the treatment of myocardial infarction at the Municipal Hospital, Solingen, Germany, was by "conventional" methods, that is, the patients were put to bed for 6 weeks, shielded from physical and psychological stress, prohibited from smoking, strictly dieted, and given analgesics. Of 239 patients so treated, 47% died. Dismayed by these poor results the authors evolved a "comprehensive" method of treatment in the next 244 cases of myocardial infarction, the conventional methods described above being supplemented with drugs designed to prevent or relieve the several complications accompanying infarction. First they at once give strophanthin (0.125 mg.) to strengthen cardiac contraction. In regard to anticoagulant drugs, the authors prefer dicoumarol given for at least 6 weeks, though in cases seen soon after infarction heparin may be used. All cases of arrhythmia, provided there are no disturbances of A-V or intraventricular conduction, are given during each 24 hours 2.5 g. of quinidine and 0.25 g. of procainamide for their antifibrillatory effect throughout the entire period of treatment. Circulatory collapse, indicated by a fall of the systolic blood pressure to under 100 mm. Hg, is treated by an intravenous drip containing 3 to 5 mg. of noradrenaline or, in milder cases, by the intramuscular injection every 4 to 6 hours of a depot preparation of noradrenaline, until the systolic pressure is stabilized at over 100 mm. Hg. Intravenous cortisone is administered if strophanthin and noradrenaline do not control the condition. Shock is treated with prednisolone (50 mg.) or dexamethasone (5 mg.) injected intravenously, and this treatment continued until all clinical manifestations of shock have disappeared.

A comparison of the 239 cases treated before 1955 (Group 1) with the 244 treated after this date (Group 2)—the two groups being comparable in regard to age and sex distribution and location of the infarct—showed that: (1) whereas the mortality in Group 1 was 47% (112 deaths), in Group 2 it was only 25% (61 deaths); (2) in both groups 50% of deaths occurred within the first 3 days, but in Group 1 27 patients died on the first day and 27 on the second or third day, whereas in Group 2 18 died on the first day and 14 on the second or third day; (3) in both groups the death rate rose with each decade of age; thus in Group 1 32% of deaths occurred in the 5th decade of life and 67% in the 8th decade, the corresponding figures for Group 2 being 14% and 38%.

While the authors are gratified that their "comprehensive" treatment lowered the over-all mortality from myocardial infarction, they point out that there is no room for complacency as long as the rate during the first 3 days remains so high. They urge that since it is usually the general practitioner who makes the initial diagnosis it is he who must initiate "comprehensive"

treatment while awaiting the patient's admission to hospital. Since infarcts occur most often in the left ventricle the early signs of decompensation appear first in the lungs and must be treated forthwith if manifest heart failure, which carries a mortality of 80%, is to be prevented. The authors consider that reports of the increased sensitivity of the infarcted heart to glucosides have been exaggerated and that strophanthin in doses of 0.125 mg. does not provoke disturbances of rhythm. Circulatory collapse is directly responsible for a large number of early post-infarction deaths. The fall in blood pressure affects the coronary circulation in particular by increasing the oxygen deficit in a heart already damaged and thus favours the continuation of thrombosis and the enlargement of the necrotic area in the myocardium.

The authors consider it important that the patient's systolic blood pressure should be raised by an intramuscular injection of depot noradrenaline before he is transported to hospital, and for post-infarction shock recommend an intravenous injection of cortisone as a "first-aid" measure in this dire emergency, in which it may be dramatically life-saving.

E. S. Wyder

VALVULAR DISEASE

369. Transventricular Mitral Commissurotomy: Surgical Technique and a Hemodynamic Evaluation of the Method

A. G. MORROW and N. S. BRAUNWALD. *Journal of Thoracic and Cardiovascular Surgery* [J. thorac. cardio-vasc. Surg.] 41, 225-235, Feb., 1961. 6 figs., 10 refs.

Transventricular mitral valvotomy has gained increasing popularity over the transatrial route in recent years. The authors have studied the haemodynamics in two comparable series treated at the National Heart Institute, Bethesda, Maryland, by measuring the change in gradient between the left atrium and left ventricle (across the mitral valve) before and after valvotomy. The two series consisted of 50 control cases operated on by the transatrial route and 25 by the transventricular operation respectively. In performing the latter a left, 6th-rib, post-lateral thoracotomy is performed and the pericardium opened. Pressures are recorded and the operator's index finger is inserted into the atrial appendage. In about 15% of cases the commissures can be opened with the finger, but in the remainder a small stab wound is made in the apex of the left ventricle and a 2-blade dilator inserted. The tip of this is guided through the valve orifice and the blades opened to 3.5 to 4 cm. along the commissure lines.

The pressure results showed that the abolition of the gradient across the valve was much better when a transventricular dilatation was performed, a mean reduction in pressure of 29% being recorded in the transatrial control cases compared with one of 62% in those subjected to transventricular valvotomy. It is considered that the reduction in gradient is a far better measure of the success of the operation than clinical appraisal. It is noted that in no case treated by transventricular valvotomy was

there evidence of regurgitation or of an increase in regurgitation if some reflux was already present before operation.

T. Holmes Sellors

370. Transventricular Mitral Valvulotomy under Controlled Hypotension

V. O. BJÖRK, M. H. HOLMDAHL and B. LÖF. *Journal of Thoracic and Cardiovascular Surgery* [J. thorac. cardiovasc. Surg.] 41, 236-243, Feb., 1961. 1 fig., 8 refs.

The authors describe, from the University Hospital, Uppsala, 150 cases of mitral stenosis, of which 83 were operated on by the transventricular route, following the method of Logan and Turner (*Lancet*, 1959, 2, 874; *Abstr. Wld Med.*, 1960, 27, 451). In 22 of the latter cases dilatation of the aortic valve was also performed. [The operative technique resembled that described by Morrow and Braunwald (see Abstract 369) except that the skin incision was subcostal.] Emphasis is laid on the use of induced hypotension during the actual cardiac manipulations, the great advantage claimed for this procedure being the ease of control and closure of the ventricular incision.

From the results of this experience the authors conclude that the transventricular route gives better splitting of the commissures than does the transatrial route although at the cost of a slightly higher incidence of regurgitation. There was an over-all operative mortality of 9% (18% if the cases in which the aortic valve was dilated were included), cerebral embolism being prominent as a cause of death.

T. Holmes Sellors

371. Five-year Follow-up Study of Closed Mitral Valvulotomy

J. G. SCANNELL, J. F. BURKE, F. SAIDI, and J. D. TURNER. *Journal of Thoracic and Cardiovascular Surgery* [J. thorac. cardiovasc. Surg.] 40, 723-730, Dec., 1960. 5 figs., 2 refs.

The authors discuss the 5-year results of closed mitral valvotomy in 100 consecutive patients surviving operation performed between 1952 and 1955 at the Massachusetts General Hospital, Boston. The series consisted of 78 females and 22 males.

Satisfactory results were obtained in 61 cases and fair to poor results in 20; 19 of the patients had died. The survival rate of 81% shows considerable improvement over the results of medical treatment in a comparable but smaller group of cases. In most of the cases with poor operative results deterioration became evident during the first year. The results were better in women than in men and also in cases where a satisfactory split of the valve had been obtained at operation. Calcified and rigid valves generally gave poor results. Reoperation has been necessary in 10 cases. The authors' total experience with 26 reoperations (8 closed and 18 open operations) for mitral stenosis is briefly reviewed.

It is suggested that the use of a mechanical dilator (Logan-Tubbs) should improve the results of valvotomy by ensuring an adequate split, especially where the valve is tough and fibrous. Where the valve is calcified better results can be expected from open operations with cardiopulmonary bypass.

F. J. Sambrook Gowar

BLOOD VESSELS

372. The Aetiology of Coarctation of the Aorta

M. CAMPBELL and P. E. POLANI. *Lancet* [*Lancet*] 1, 463 468, March 4, 1961. 28 refs.

The authors, at Guy's Hospital, London, have made a detailed analysis of 151 patients with coarctation of the aorta, with particular reference to associated abnormalities both in the patients and in their families. There were 95 males and 56 females (sex ratio 1.7:1) and their associated cardiac abnormalities were as follows: aortic regurgitation in one-quarter (sometimes found at necropsy to be due to a bicuspid valve), patent ductus (7 cases), aortic stenosis (6), major abnormalities of aortic branches (5), and mitral incompetence (3); 12 had other cardiac malformations than those listed above. Among the 19 non-cardiac malformations were 3 examples of Turner's syndrome (webbing of neck, gonadal dysplasia, female habitus, and male chromosomes).

A total of 252 sibs were traced. Only one had a cardiac malformation, but 7 had other abnormalities—that is, 2.8% compared with a normal of under 1%. Among the 49 children of propositi were 2 with cardiac malformations, which is a high incidence, although many of these families are as yet incomplete.

Parents of propositi had no more malformations than might be expected by chance. There was no consanguinity such as would argue the inheritance of a Mendelian recessive trait. Neither maternal age nor birth order influenced significantly the incidence of coarctation. The mean difference between paternal and maternal ages was a little greater than normal (2.87 against 2.3 years), which, it is suggested, may have a genetic influence.

Boys with coarctation did not differ from their sibs in their birth weight, but were born in slightly greater numbers in March and April. Affected girls had a significantly lower birth weight than their sibs and were born more often in August to October. Purely in speculation, the authors consider the possibility of a link between maleness and excessive muscular contraction of the aortic wall near the point of entry of the ductus contrasted with a link between femaleness and a lack of such contraction, causing persistence of the patent ductus.

J. A. Cosh

373. Coarctation of the Aorta with Particular Emphasis upon Improved Techniques of Surgical Repair

G. C. MORRIS JR., D. A. COOLEY, M. E. DEBAKEY, and E. S. CRAWFORD. *Journal of Thoracic and Cardiovascular Surgery* [J. thorac. cardiovasc. Surg.] 40, 705-722, Dec., 1960. 12 figs., 22 refs.

The authors report 171 cases of aortic coarctation treated surgically, with an operative mortality of 4.6%, at 3 hospitals in Houston, Texas. Nearly half the patients were over the age of 20, while among the rest were 19 children under one year of age. The procedures used were as follows. (1) End-to-end anastomosis (98 cases, or 58%)—most commonly used in children and young adults with short "adult" or post-ductile stenosis.

(2) Wedge resection and repair (5 cases, or 3%)—occasionally used for short isthmic coarctations in young patients. (3) Resection and graft replacement (end-to-end) (60 cases, or 35%)—used for (a) long coarctations of the "infantile" or preductile type; (b) coarctation involving the aortic arch with stenosis extending proximal to the subclavian artery; (c) sub-isthmic coarctations involving the middle and lower thirds of the descending thoracic or upper abdominal aorta; and (d) any type in which local degenerative changes make direct anastomosis hazardous. (4) Aortic bypass by means of "dacron" graft (8 cases, or 4%)—in (a) situations where resection may be hazardous; (b) poor-risk cases; (c) cases of long segmental involvement or multiple areas of stenosis; and (d) coarctations involving the lower thoracic and upper abdominal aorta.

Dacron grafts have been used extensively for over 5 years and have proved eminently satisfactory, not only because of ease in handling, but also on the grounds of long-term reliability. No degenerative complications have been encountered.

F. J. Sambrook Gowar

374. Physical Activity and Atherosclerosis. Study of the Presence of Signs of Atherosclerosis in a Group of Individuals from a Mountainous Area. (Attività fisica ed aterosclerosi. Studio sulla presenza dei segni di aterosclerosi in un gruppo d'individui di montagna)

L. BERTONI, R. BISTAFFA, L. BONAZZI, S. GARBIN, L. MARCONI, and A. VITTONI. *Cardiologia pratica [Cardiol. prat. (Firenze)]* 11, 612-624, Dec., 1960 [received April, 1961]. 19 refs.

The hardy mountaineers living in the Alpine valleys of Northern Italy enjoy a reputation of almost complete freedom from myocardial infarction and angina pectoris. To confirm this, 53 men aged 16 to 84 years who normally lived at an altitude of 1,400 metres (4,600 ft.) and were employed as guides, forest workers, or porters were systematically examined by a team from the Verona hospitals.

Careful family histories were taken and anthropometric measurements made. Dietary habits and consumption of alcohol and tobacco were ascertained and classified in three grades. In addition to clinical examination, including that of the ocular fundi, the following investigations were carried out in all cases: the electrocardiogram recorded, the serum cholesterol level assessed, plasma lipids analysed electrophoretically, and the colloidal state of the serum and coagulation times estimated.

The findings, judged by the men's clinical condition and results of the above tests, showed a high degree of normality of the circulatory system, more remarkable in view of the habitual high proportion of animal fat in the diet and the heavy consumption of alcohol and tobacco disclosed by the group. In the authors' opinion heavy physical activity, absence of modern stresses of life, and the prevalence of a mesomorphic constitution are the protective elements preventing the development of atherosclerosis.

[The tables of the findings quoted in the text are unfortunately not reproduced.]

A. J. Karlish

375. Ten-year Status after Sympathectomy for Arteriosclerosis

E. A. EDWARDS and C. CRANE. *Journal of the American Medical Association [J. Amer. med. Ass.]* 175, 677-679, Feb. 25, 1961. 1 fig., 7 refs.

Ten years ago the authors reported (*New Engl. J. Med.*, 1951, 244, 199; *Abstr. Wld Surg.*, 1951, 10, 87) the results of lumbar sympathectomy in 100 cases of arteriosclerosis of the legs (27 in diabetics) treated at the Peter Bent Brigham Hospital, Boston, Massachusetts. Since then a 5-year follow-up has been published (*A.M.A. Arch. Surg.*, 1956, 72, 32), and the present paper extends the period of observation to 10 years. At the end of the first 5 years there were 65 survivors, but 23 patients have since died, 17 of them from visceral arteriosclerosis. It is noteworthy that the 42 patients remaining alive after 10 years had a preoperative incidence of severe visceral disease and diabetes only about one-half that of the group as a whole; in respect of age, sex, and site of arterial obstruction they differed little from the rest of the series. Of the 42 patients, 35 (83%) had good or fair function of their legs ("fair" indicating moderate restriction due to claudication). This represents a deterioration of about 10% from the status at 5 years; 5 major amputations were required during the second quinquennium. It is of interest that all the other major amputations (10 cases) in the series were needed because sympathectomy proved inadequate, and were performed within a few months of the sympathectomy. Of the 21 survivors under 65 years of age, 15 were active and comfortable, whereas only 10 of the 21 over 65 came into that category, the difference being due to the greater prevalence of visceral disease in the latter group.

The authors consider that deterioration in a limb was not the result of return of sympathetic function, but of further arterial occlusion; furthermore, they suggest that the infrequency of such occlusion over the 10-year period points to a retarding effect of sympathectomy on the occlusive process. [This seems to the abstractor to be purely speculative.]

C. J. Longland

HYPERTENSION

376. The Role of Heredity in the Aetiology of Hypertensive Vascular Disease. (Роль наследственности в этиологии гипертонической болезни)

I. A. RYVKIN. *Клиническая Медицина [Klin. Med. (Mosk.)]* 38, 24-29, Dec., 1960. 13 refs.

In hypertensive vascular disease the importance of the hereditary factor has been shown to be greater in the families of male than of female patients and in those of young than of elderly hypertensives. It is this inherited predisposition which is responsible for the appearance of the disease at an earlier age and in a more severe form. This study of 600 patients and 587 of their children and siblings, as well as 662 healthy controls, showed that the incidence of stroke or sudden death of the parents or the incidence of the disease among near relatives of hypertensive patients was 4 to 5 times higher than among those of the controls. Also the incidence of

stroke, sudden death, and other fatal cardiovascular lesions occurring below the age of 60 was more common among the relations of male (10.7%) than female (7.6%) patients. It was also shown that when both parents suffered from hypertensive disease the probability of a fatal cardiovascular lesion, stroke, or sudden death in the offspring was 3 times as great as in absence of such a parental history (12.1 and 4% respectively). When only one parent had such a history the chances were 7.7% and 5.7% respectively.

In a further study 338 close relatives of hypertensive patients, aged between 18 and 40 years and with a mean blood pressure of 140/90 mm. Hg., were investigated for evidence of pre-hypertensive changes. In this group labile blood pressure and various vasomotor disturbances were 1½ times to twice as common as among the healthy controls.

A follow-up study of 507 subjects for various periods averaging 10 years revealed that the incidence of hypertensive disease among the relatives of hypertensives and those of the controls was 37.8% and 7.9% respectively.

S. W. Waydenfeld

377. Diet in the Treatment of Hypertensive Disease. (Диетотерапия гипертонической болезни)
E. I. DORONOVA and V. P. NIKITIN. *Клиническая Медицина* [Klin. Med. (Mosk.)] 38, 34-38, Dec., 1960. 3 figs., 17 refs.

In hypertensive disease of Grade II or III treatment with hypertensive drugs or combinations of these drugs frequently fails to produce the desired result, and consequently venesection often becomes necessary to prevent hypertensive crises. The effects of this procedure are, however, short-lived and a diet of sugar and fruit is widely used after venesection in an attempt to prolong the results of the latter. The patients are given on 2 consecutive days after the venesection 200 g. of sugar, not more than 400 g. of fruit, and 250 ml. of tea to drink daily.

Of 60 patients so treated, 56 with hypertension of Grade II and 4 of Grade III, 17 failed to respond, but 43 improved considerably and the blood pressure was markedly reduced. However, in 27 cases the effect lasted for 2 days only (that is, while receiving the diet) and for only up to 4 days in the other 16. This hypotensive effect of the diet, which has been observed also in absence of the preliminary venesection, may possibly be due to adrenal inhibition resulting from the grossly reduced intake of sodium ions (daily output of chlorides is reduced to about 1 g.).

The authors have therefore investigated the effect of a high-potassium diet, composed mainly of oats, beans, peas, rice, curd cheese, sour cream, flour (70%), melted butter, vegetables, and fruit or jam, providing some 2,500 Calories daily, with 0.3 to 0.6 g. of sodium and 3.7 to 4.67 g. of potassium. This diet was instituted when drug treatment had failed and was continued for 12 to 15 days. No diuresis, loss of weight, or changes in the blood residual nitrogen or indican were observed. A majority of the 75 patients so treated, of whom 61 had hypertension of Grade II, improved subjectively, and the blood pressure was reduced in 54 cases (from a range of 220-200/130-100

mm. Hg to 160-120/70-75 mm. Hg in 28 and by 20 to 30 mm. systolic and 5 to 10 mm. Hg diastolic in 26). In 39 cases, however, the hypotensive effect lasted only while taking the diet, but in 15 patients it was more stable and the blood pressure was still reduced at the time of discharge from hospital. No effect was noted in 21 patients (7 with Grade-III and 14 with Grade-II disease), some of whom resented the diet, which thus had an opposite effect to that desired, while 5 patients actually developed hypertensive crises while taking the diet.

S. W. Waydenfeld

378. Essential Hypertension and Aldosterone

E. H. VENNING, I. DYRENFURTH, J. B. DOSSETOR, and J. C. BECK. *Circulation* [Circulation] 23, 168-176, Feb., 1961. 5 figs., 22 refs.

In this study of the role of aldosterone in essential hypertension, reported from McGill University, Montreal, urinary aldosterone was extracted after acid hydrolysis and the fraction containing aldosterone isolated by paper chromatography and measured by reduction with blue tetrazolium. The tetrahydro derivative of aldosterone was hydrolysed by β -glucuronidase, isolated, and its amount determined after acetylation by the reduction of blue tetrazolium.

In 72 normotensive subjects receiving a daily sodium intake of 100 to 170 mEq. the daily urinary excretion of aldosterone ranged from 2.0 to 12.0 (mean 5.1) μ g. In 22 patients with essential hypertension but without renal disease it ranged from 3.3 to 18.9 (mean 8.8) μ g., and in 5 such patients with renal disease it was 5.4 to 14.3 (mean 10.1) μ g. In 2 patients with malignant hypertension the daily aldosterone excretion levels were 12 and 18 μ g. respectively. The tetrahydro derivative was also excreted in larger amounts by patients with essential hypertension than by normal subjects, and hypertensive patients showed wider fluctuations in their daily excretion of aldosterone than the controls. The administration of ACTH (160 units over 48 hours) produced similar increases in urinary 17-hydroxycorticosteroid and aldosterone excretion in normotensive subjects and patients with essential hypertension, suggesting that the adrenal glands of hypertensive patients are not more responsive to the hormone than those of non-hypertensives. In 2 patients who died of malignant hypertension analysis of the adrenal glands showed normal or low values for hydrocortisone, normal values for cortisone, but very high levels for aldosterone.

K. G. Lowe

379. Study of the Basal Excretion of Aldosterone in 19 Cases of Hypertension. (Étude de l'excrétion basale de l'aldostérone dans 19 cas d'hypertension artérielle)

— ALBEAUX-FERNET and J. D. ROMANI. *Bulletin de l'Académie nationale de médecine* [Bull. Acad. nat. Méd. (Paris)] 145, 128-133, Feb. 7, 1961. 1 fig., 7 refs.

The daily urinary excretion of aldosterone, determined chromatographically, in a group of 19 hypertensive patients was found to range from 3 to 30 μ g. (mean 14 μ g.) in the 24 hours. In a group of normal subjects [number not stated] the average excretion was 6.4 μ g. in 24 hours. In older patients in whom the hypertension

was attributed to atheroma the values for aldosterone excretion were within the normal range, but elevated values were obtained when hypertension was associated with obesity. Marked variability in the daily excretion of aldosterone was a characteristic finding in hypertensive patients and was considered to be an unfavourable prognostic sign.

[This study suffers from a lack of detail in the presentation of important clinical data.] *Bernard Isaacs*

380. The Prolonged Treatment of Hypertension with Guanethidine

I. H. PAGE, R. E. HURLEY, and H. P. DUSTAN. *Journal of the American Medical Association [J. Amer. med. Ass.]* 175, 543-549, Feb. 18, 1961. 3 figs., 17 refs.

The antihypertensive effects of guanethidine seem to result from its ability to depress sympathetic vasomotor function either by decreasing norepinephrine [noradrenaline] production by nerve endings or by releasing catecholamines from heart and blood vessels.

Guanethidine has proved to be an effective drug for the treatment of hypertension for periods as long as 18 months. Of 38 patients with renal or essential hypertension, reduction of supine diastolic pressure to levels of less than 105 mm. Hg for weeks or months was achieved by guanethidine in 22 patients; 5 of these developed edema which was easily eliminated by an orally administered diuretic. Twelve other patients, who originally received guanethidine only, failed to respond satisfactorily but achieved good blood pressure control with additional therapy, either as hydralazine, or an oral diuretic. One patient in whom guanethidine treatment reduced supine arterial pressure to 108 mm. Hg, did not receive other antihypertensive drugs.

Three patients with severe diastolic hypertension were given guanethidine alone at first; in one it caused only an orthostatic hypotension but when hydralazine was added supine diastolic pressure was reduced from 131 mm. Hg to 112 mm. Hg; in the other 2 guanethidine lowered supine diastolic pressure about 25 mm. Hg from levels of 140 to 150 mm. Hg, and addition of hydralazine had no further hypotensive effect.

To reduce supine arterial pressure to almost normal levels, severe orthostatic hypotension was usually produced during the first weeks of treatment. With reduction in the dose of drug and elastic stockings, it was possible to overcome the incapacitating hypotension without loss of supine blood pressure control.

The only major side-effect of guanethidine was diarrhea, which was easily controlled with atropine. Tolerance to the drug has not appeared.—[Authors' summary.]

381. Adrenergic Blocking Agents in the Treatment of Hypertension

F. W. WOLFF. *Journal of Chronic Diseases [J. chron. Dis.]* 13, 133-147, Feb., 1961. 1 fig., 7 refs.

This paper from Johns Hopkins University School of Medicine, Baltimore, Maryland, purports to compare the hypertensive effect of bretylium tosylate ("darenthin")

with that of guanethidine ("ismelin") in 50 patients with hypertension. Both drugs were found to be potent and to have few side-effects. Guanethidine is preferred in view of its longer action, but marked tolerance to the drug developed within 3 to 9 months; this also occurred with bretylium.

[Although both the drugs were given to each patient at different times the paper does not set out the comparative data in a form which makes it possible to abstract them.] *H. F. Reichenfeld*

382. A Study of 38 Patients and Their Responses to Guanethidine: a New Antihypertensive Agent

J. T. EAGAN and E. S. ORGAIN. *Journal of the American Medical Association [J. Amer. med. Ass.]* 175, 550-553, Feb. 18, 1961. 3 figs., 10 refs.

Thirty-eight patients received guanethidine orally over an average period of 19 weeks in divided doses. Therapy generally was begun with small initial doses, 5 to 10 mg. twice daily, with increments in dosage made gradually, depending upon reduction in blood pressure and elimination or control of annoying side effects. The blood pressure fell in all but 9 patients recumbent and 3 erect. A significant fall in mean blood pressure of 20 mm. Hg or more was noted in 9 patients (23%) recumbent and 22 patients (58%) standing, thus pointing out the greater postural effect of the drug. Mild side effects were seen in 33 patients (87%) but were severe enough to discontinue treatment in only 5 (13%). Side effects generally could be alleviated or abolished by reduction of the total daily dose. No serious toxic effects were seen, although one patient developed disseminated lupus erythematosus while on treatment; this disease was not attributed to the drug.

Guanethidine would appear to have definite but limited utility as an antihypertensive agent for the more severely hypertensive patient because of its marked postural effect on blood pressure and the incidence of its side effects. Final conclusions regarding the ultimate usefulness of the drug, administered alone and in combination with other agents, must await more extended experience.—[Authors' summary.]

383. Relation of Hypertension to Unilateral Renal Atrophy: a Study of Necropsy Records

H. J. BARRIE, A. I. MACRAE, and S. M. SHEA. *Lancet [Lancet]* 1, 193-195, Jan. 28, 1961. 4 refs.

The relationship between unilateral renal disease and hypertension was studied in the records of 5,000 consecutive necropsies performed at the Banting Institute, University of Toronto. In this series there were 106 cases of renal atrophy, which was due to stenosis of the main vessels in 11 cases, to chronic pyelonephritis in 34, to obstruction of the urinary tract in 37, and to multiple infarcts in 24. The blood pressure in these cases was noted. Severe hypertension was present in all the cases of stenosis of the renal artery, while of the 39 cases of malignant hypertension in this large series, 1 in 6 was associated with unilateral renal atrophy.

J. B. Wilson

Clinical Haematology

384. **Splenectomy in Werlhof's Disease (Purpura Haemorrhagica).** (К вопросу о спленэктомии при болезни Верльгофа)

A. G. VORONIN, S. M. JUS'KO, and Z. P. ZORINA. *Педиатрия [Pediatrija]* 40, 16-18, Feb., 1961. 7 refs.

The indications for splenectomy in purpura haemorrhagica are not clearly defined, and in the acute phase the risk is considerable. In the authors' opinion the operation should, if possible, be deferred until the disease shows a remission, since during this time the postoperative mortality is much lower; the operation should be preceded by blood transfusions. If, however, the patient's condition continues to deteriorate in spite of conservative measures the risk of operation must be accepted. In 2 such cases in the authors' series, both in children, it was life-saving; after operation the thrombocyte count rose within 24 to 48 hours from 10,000 to over 100,000 per c.mm., later remaining at about 50,000 to 60,000 per c.mm. for several months; haemorrhage did not recur.

L. Firman-Edwards

385. **The Use of Quinine in Solutions for the Preservation of Blood.** (Užití chininu jako přísady roztoků ke konservaci krve)

J. FIALA and E. DOBRÝ. *Vnitřní lékařství [Vnitřní Lék.]* 7, 147-153, Feb., 1961. 12 refs.

Prolongation of the life of erythrocytes in stored blood can be achieved by slowing down the metabolic processes in the cells either by cold storage or by the addition of certain substances which inhibit the enzymatic systems of the erythrocyte. It is well known that quinine blocks certain enzymatic and metabolic reactions and also reduces the permeability of cell membranes, and it has been claimed in Russia that the addition of quinine to the standard acid-glucose-citrate solution delays the haemolysis of the erythrocytes, which are stated to remain active for 50 to 60 days after the addition of quinine. The present authors, however, could find no published confirmation of this claim and have therefore made an independent investigation, comparing the results of transfusions with blood preserved with the Russian solution with those with blood preserved by the standard method used in Czechoslovakia.

The Russian solution contained 5 ml. of a 2% solution of quinine dihydrochloride in each 100 ml. Transfusions carried out with blood preserved with this solution produced reactions in 26% of cases compared with only 0.5% when the standard acid-glucose-citrate solution was used. It is also pointed out that transfusions containing quinine may induce miscarriage in pregnant women. No qualitative improvement was found after adding quinine to the blood preservation solution and it was therefore concluded that this modification increases the risk of reaction in the patient and has no compensating advantage.

Paul Frankl

386. **Contribution to the Study of the Properties of Preserved Blood Oxygenated with Hydrogen Peroxide.** (Příspěvek ke studiu vlastností konservované krve okysličené peroxydem vodíku)

J. FIALA and M. VLČKOVÁ. *Vnitřní lékařství [Vnitřní Lék.]* 7, 257-264, March, 1961. 4 figs., 33 refs.

The authors state that it has been reported in the literature that transfusions with arterial or artificially oxygenated blood give much better therapeutic results than transfusions with venous blood, oxygenated blood exerting a powerful stimulus on the blood pressure and breathing centre and on erythropoiesis. The main indications for the use of oxygenated blood are said to be shock, severe blood loss, an open pneumothorax, major operations, and myocardial infarction. As it is technically rather difficult to obtain arterial blood, various methods of oxygenating venous blood have been used, most of them employing oxygen from a cylinder. A simpler method, however, is stated to be to add a 3% solution of hydrogen peroxide (H_2O_2) to the preserved blood.

The authors have investigated the latter method and found that oxygenation with H_2O_2 did not make any marked improvement in the quality of the blood, but that it also had no deleterious effect, 93.5% of the erythrocytes surviving 3 days after transfusion. A comparison of the coagulation of oxygenated and venous blood after 14 days' storage showed that the former clotted more slowly than the latter as thrombin and thrombokinase are inactivated by oxygenation, which reduces the pH of the blood. However, the difference was not significant. On the basis of the authors' clinical experience there is only very little difference in the action of arterial blood, venous blood, and blood oxygenated with H_2O_2 on transfusion.

Paul Frankl

ANAEMIA

387. **The Role of the Erythropoietic Hormone in Anaemia** D. G. PENINGTON. *Lancet [Lancet]* 1, 301-307, Feb. 11, 1961. 1 fig., bibliography.

The author of this paper from the London Hospital, after giving a valuable critical review of the methods used to assay erythropoietic hormone, describes the results of such assay in plasma from patients severely anaemic from a variety of causes. For this purpose he used ^{59}Fe utilization in rats rendered polycythaemic by intraperitoneal injections of packed erythrocytes from animals of the same species. The titre was consistently raised in plasma from iron-deficiency, megaloblastic, haemolytic, and aplastic types of anaemia, and in the plasma from patients with anaemia due to leukaemia, infection, rheumatoid arthritis, and malignant disease.

The highest hormone levels were found where erythropoiesis was considerably slowed, and lower levels were demonstrated where erythropoiesis was more rapid—a finding which suggests that the low plasma levels may be due to utilization of the hormone by an active bone marrow. Plasma from patients severely anaemic as a result of chronic renal insufficiency failed to show increase in erythropoietic activity of comparable degree. A method is described for concentration of erythropoietic hormone in plasma. With this procedure erythropoietic hormone could not be demonstrated in normal plasma, but was found in a normal subject after venesection to a level of 87% haemoglobin. No evidence was found of urinary loss of hormone in chronic renal insufficiency, although hormone activity was found in the urine of other severely anaemic patients; nor was there evidence of suppression of hormone activity by uraemic plasma. It is concluded that defective production of erythropoietic hormone is an important factor in the development of the anaemia of chronic renal insufficiency, but that it is not the sole one.

[This is an excellent paper which should be studied in the original for technical details.]

J. L. Markson

388. Effect of Food on Absorption of Radioactive Vitamin B₁₂

D. J. DELLER, H. GERMAR, and L. J. WITTS. *Lancet* [Lancet] 1, 574-577, March 18, 1961. 2 figs., 26 refs.

The influence of food on the absorption of radioactive vitamin B₁₂ was studied at the Radcliffe Infirmary, Oxford, in 10 control subjects, 5 patients with pernicious anaemia in remission, and 21 patients who had undergone partial gastrectomy one to 18 years previously; of these last, 10 had previously been shown to have impaired absorption of vitamin B₁₂ and in 13 the serum vitamin level was below the lower limit of normal. For the tests 0.5 µg. of ⁵⁸Co-labelled vitamin B₁₂ was first administered after a 12-hour fast and again, at least 2 weeks later, together with a standard meal containing no vitamin B₁₂; absorption of the vitamin was estimated by determining the difference between the amount of radioactivity given by mouth and that excreted in the faeces. If the absorption of vitamin B₁₂ was found to be impaired in the first (fasting) test, a third test was carried out in which the same dose was given together with intrinsic factor.

In the control subjects and the patients with pernicious anaemia there was no significant difference in vitamin-B₁₂ absorption as between the results of the fasting and food tests. However, of the 21 patients who had had a partial gastrectomy, 20 showed significantly better absorption of the vitamin when it was given with food, whether or not absorption had been impaired in the fasting state. In some of these patients with grossly abnormal vitamin absorption the enhancement obtained by taking the vitamin with food was similar to that achieved by giving it with intrinsic factor. The possible mechanisms of the enhancing action of food are discussed, and the findings are contrasted with those of absorption studies of radioactive iron in patients who have undergone partial gastrectomy; in these the absorption of iron is diminished by food.

J. L. Markson

389. Pernicious Anaemia in Childhood

H. P. LAMBERT, T. A. J. PRANKERD, and J. M. SMELLIE. *Quarterly Journal of Medicine* [Quart. J. Med.] 30, 71-90, Jan. [received March], 1961. 8 figs., 37 refs.

From a review of the literature it is concluded that only 7 cases of pernicious anaemia in childhood reported can be accepted; in the others the diagnostic criteria nowadays demanded had not been satisfied—in particular steatorrhoea (especially in a latent form) had not been excluded. The authors add 2 further cases, those of a brother and sister in whom the essential feature of lack of intrinsic factor was established without doubt. One child did have features indicating the presence of a malabsorption syndrome as well, but these disappeared after treatment with vitamin B₁₂ (cyanocobalamin) and evidence is discussed which could indicate that vitamin-B₁₂ deficiency may itself lead to temporary malabsorption.

In spite of the deficiency of intrinsic factor in pernicious anaemia in childhood the authors stress the point that the expected gastric atrophy and achlorhydria do not occur, so that two of the generally accepted criteria for "true" pernicious anaemia are not satisfied. There is a strong genetic factor in the childhood cases and it is suggested that the primary defect in true pernicious anaemia is a lack of intrinsic factor, the gastric atrophy and achlorhydria perhaps appearing later either as a result of the intrinsic-factor defect or because of other agencies. The possibility that the children are homozygous for some hereditary factor is mentioned, but there is no supporting evidence as yet. The very remarkable acceleration of growth and mental development after vitamin-B₁₂ therapy is stressed; the haematological responses are excellent.

R. B. Thompson

390. Oral Treatment of Pernicious Anaemia: Further Studies

F. S. MOONEY and J. G. HEATHCOTE. *British Medical Journal* [Brit. med. J.] 1, 232-235, Jan. 28, 1961. 4 figs., 28 refs.

It is suggested that pernicious anaemia is due not to deficiency of "intrinsic factor" as currently understood, but to a failure of gastric proteolysis in the absence of a protein-bound form of vitamin B₁₂ (cyanocobalamin). Cases of pernicious anaemia have been successfully treated by the authors with an oral vitamin-B₁₂-peptide complex derived from *Streptomyces griseus*, as previously described (*Lancet*, 1960, 2, 291; *Abstr. Wld Med.*, 1961, 29, 95).

In the present paper they now report the clinical results obtained with a new peptide complex derived from fermentations of a species of *Propionibacterium*. The ratio (on a weight basis) of vitamin B₁₂ to peptide in various batches of the preparation varied from 1:3.7 to 1:7.1, indicating that it was not a chemical compound in the strict sense, but rather a loose combination of peptide and vitamin which can occur in different proportions. One batch, designated H.P.P./4, was found to be approximately as effective as folic acid in bringing about the maturation of megaloblasts. A relatively high initial dose given to 11 patients for a short period was

followed by a maintenance dose (in terms of vitamin B₁₂) of about 10 µg., which was increased when necessary up to 30 or 40 µg. In 10 cases maintenance over a long period (849 days) was possible on an average daily dose equivalent to 19.7 µg. of vitamin B₁₂, compared with the generally agreed requirement of 100 µg. daily of crystalline vitamin B₁₂, of which, it is suggested, probably only 1% is absorbed into the haematopoietic system. In 2 cases a maximum response was obtained with a daily dosage of 300 µg. of vitamin-B₁₂ equivalent. No case of refractoriness and no neurological complications developed and all patients have remained in complete remission.

Ethel Browning

391. **Thyrotoxicosis Associated with Pernicious Anemia**
G. P. McNICOL. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] **241**, 336-342, March, 1961. 18 refs.

It was noted that a surprisingly large number of patients with pernicious anaemia attending the blood clinic of the Glasgow Royal Infirmary were or had been thyrotoxic. A careful study was therefore made of 100 consecutive patients with pernicious anaemia. There were 7 with a history of thyrotoxicosis, while the "thyrotoxicosis diagnostic index" of Crooks *et al.* (*Quart. J. Med.*, 1959, **28**, 211; *Abstr. Wld Med.*, 1959, **26**, 300) was on average -1.37 compared with -5.38 for a control group of hospital patients with other conditions. This difference was significant and remained so when the values for those patients with active thyrotoxicosis were excluded from the group with pernicious anaemia.

Of the 256 patients with pernicious anaemia attending this clinic between 1950 and 1959, 13 (5.1%) had or had had thyrotoxicosis, a figure significantly higher than that for a control group of 256 hospital patients without pernicious anaemia, in which there were only 2 with past or present thyrotoxicosis (0.78%). In only one case did the thyrotoxicosis precede the pernicious anaemia. Proportionally more women than men appeared to have the combination, but the difference was not significant statistically. The cause of the relationship remains unexplained.

A. Gordon Beckett

LEUKAEMIA

392. **The Antigenicity of Normal and Leukemic Human Leukocytes**
T. E. BRITTINGHAM and H. CHAPLIN JR. *Blood* [Blood] **17**, 139-165, Feb., 1961. 2 figs., 25 refs.

In 1954 the first named of the authors of this paper from Washington University School of Medicine, St. Louis, was successfully immunized against the leucocytes of a patient with chronic myeloid leukaemia. This resulted in the appearance in the recipient's serum of a leucocyte iso-agglutinin which was active against normal leucocytes as well as those from patients with either chronic myeloid leukaemia or chronic lymphatic leukaemia. The antibody was not, however, active against the immunized subject's own leucocytes or immature leucocytes from patients with acute leukaemia. The

presence of the antibody was first detected after the 5th weekly injection of the donor's whole blood and was detectable for at least 5 months after the 10th and final injection. Also, 18 months after the last injection of leukaemic blood the leucocyte iso-agglutinin was re-stimulated by the administration of a very much smaller volume of normal leucocytes. The character of this response was not that of a primary immunization.

The recipient was then re-immunized a second time 15 months after the last injection of normal blood, on this 3rd occasion whole blood from a second donor with chronic myeloid leukaemia being used. The first 6 injections produced no symptoms in the recipient and no significant change in his total leucocyte count. Thereafter, however, he experienced a mild clinical reaction to each injection and his leucocyte count showed an initial fall, followed by a transient leucocytosis. The administration to the leukaemic donor of the author's plasma, known to contain the leuco-agglutinin, was without effect, but the use of the gamma-globulin fraction of a much larger volume of plasma may have had a transient effect on the leukaemia, as previously described (*Cancer*, 1960, **13**, 412). Careful observation of the normal recipient has revealed no evidence of the transmission of chronic myeloid leukaemia by the infusion of leukaemic blood.

These and other observations are discussed at some length. It is concluded that viable leucocytes are an effective, if complex, antigen. No evidence was obtained of the existence of a serum leucocytosis factor in chronic myeloid leukaemia. The normal total leucocyte count in the immunized subject, in the presence of a powerful iso-agglutinin active against leucocytes, suggests that agglutinating leucocyte iso-antibodies can play little part in the genesis of the chronic leucopenic states.

A. G. Baikie

393. **A Study of Prednisone Therapy in Chronic Lymphocytic Leukemia**

R. K. SHAW, D. R. BOGGS, H. R. SILBERMAN, and E. FREI III. *Blood* [Blood] **17**, 182-195, Feb., 1961. 28 refs.

This controlled study was carried out at the National Cancer Institute, Bethesda, Maryland, to determine the antileukaemic effect of prednisone in chronic lymphatic leukaemia and also its effect, when used in that disease, on the frequency and character of infections. Of 24 consecutive new patients with chronic lymphatic leukaemia referred to the Institute, 18 were selected for study; the other 6 cases were excluded for valid reasons and it is considered that their exclusion was unlikely to have influenced the essential conclusions of the study. The 18 patients were assigned at random to two groups, of which the first were given prednisone for 12 weeks followed by a 12-week observation period, while for the second group the order of treatment and observation was reversed. The daily dosage schedule was 1 mg. per kg. body weight for 4 weeks, then 0.5 mg. per kg. for 4 weeks, and finally 0.25 mg. per kg. for 4 weeks; this dosage was increased in the event of infection.

Symptomatic improvement was uniformly observed and persisted after cessation of treatment in 12 cases. The initial regression of splenomegaly, hepatomegaly,

and lymphadenopathy was striking, but in most of the patients enlargement of these organs recurred either before the end of prednisone therapy or within 4 weeks of its cessation. Of 18 patients, 16 showed an increase in the total leucocyte count, which was at its maximum after 2 weeks of treatment, owing to an increased number of lymphocytes. This increase regressed before treatment was stopped and 2 months after the end of treatment the total leucocyte count was significantly below pre-treatment levels. The haemoglobin level and platelet and neutrophil counts all rose during treatment, but the increase did not persist after its withdrawal. Changes in the serum gamma-globulin level were extremely variable and could not be related to either the clinical or haematological state. It was found that the beneficial effects of a course of prednisone therapy could be obtained a second time if treatment was repeated.

A total of 13 infections occurred in 12 patients. The frequency of infection was not significantly greater in the treatment group than in the control group, but during treatment infections were generally more severe and more difficult to control. During the study 2 patients died, one of miliary tuberculosis and one of bacterial pneumonia and bleeding duodenal ulcer, and it was necessary to discontinue treatment in 2 others. Because of the transient nature of the antileukaemic effects of the steroid and especially because of the risk associated with increased severity of infections the authors conclude that prednisone should be used in chronic lymphatic leukaemia only in the treatment of haemolytic anaemia, significant thrombocytopenia, or advanced disease with bone-marrow failure.

A. G. Baikie

394. Cytogenic Studies in Chronic Myeloid Leukaemia and Acute Leukaemia Associated with Mongolism

I. M. TOUGH, W. M. COURT BROWN, A. G. BAIKIE, K. E. BUCKTON, D. G. HARNDEN, P. A. JACOBS, M. J. KING, and J. A. MCBRIDE. *Lancet [Lancet]* 1, 411-417, Feb. 25, 1961. 2 figs., 10 refs.

Although in leukaemia the total number of chromosomes is normal, the finding that one chromosome was abnormally small has been reported in certain cases of the disease. This chromosome, which is designated Ph¹ because it was first observed in a Philadelphia laboratory, is one of the 4 small acrocentric chromosomes occurring in two pairs and numbered 21 and 22 in the Denver classification. The present studies were carried out at the Western General Hospital, Edinburgh, on blood leucocytes from 18 patients with chronic myeloid leukaemia, in 3 of whom acute leukaemia had developed; the culture technique was a modification of Moorhead's method. Certain practical problems and difficulties of interpretation are discussed. Among the cases described is one in which there was sex chromosome mosaicism of the XY/XXY type and another of a patient in an acute leukaemic phase who had a second stem-line of cells characterized by a chromosome count of 49 and the chromosome changes induced by radiotherapy.

The Ph¹ chromosome has not been seen in any patient who has not suffered from chronic myeloid leukaemia; it was found in 12 of the 15 patients with the chronic

disorder in the series, but for some unknown reason in only one of the 3 patients with the acute, terminal, form of the disease. The chromosome was also not found in 3 treated cases of chronic myeloid leukaemia which ran an unusually benign course. In 5 cases of acute leukaemia in patients with mongolism (in which condition there is an increased susceptibility to acute leukaemia) only the usual chromosome abnormality associated with that condition was found, although the same chromosome (No. 21) seems to be involved as in chronic myeloid leukaemia. It is tentatively postulated that the Ph¹ chromosome may have "resulted from either a deletion or a translocation involving this chromosome, which may carry on it a genetic locus concerned with leucopoiesis".

R. B. Thompson

395. Busulfan in the Treatment of Chronic Myelocytic Leukemia. The Effect of Long Term Intermittent Therapy

A. HAUT, W. S. ABBOTT, M. M. WINTROBE, and G. E. CARTWRIGHT. *Blood [Blood]* 17, 1-19, Jan., 1961. 9 figs., 28 refs.

In this paper from the College of Medicine, University of Utah, Salt Lake City, the authors describe the results of treatment of chronic myelocytic leukaemia with busulphan. Altogether 30 patients, 24 of whom had had no earlier therapy, were given 114 courses of busulphan; 2 or more courses were given to 23 patients and 6 or more courses were given to 8 patients. The drug was mostly given in single doses of 4 to 6 mg. each morning and was usually continued until the leucocyte count fell to 10,000 per c.mm. or less. Length of remission was estimated from the termination of a course of therapy until treatment was restarted; this was generally when the leucocyte count reached 50,000 per c.mm.

Improved well-being and loss of sternal tenderness was often apparent within 2 to 3 weeks of starting treatment; about the same time the spleen (initially palpable in 27 cases) began to decrease in size and continued to do so for 3 to 8 weeks after treatment was stopped. Within 2 to 3 weeks there began an exponential fall in the leucocyte count and a rise in the packed erythrocyte volume. Initial thrombocytopenia was rare and was not regarded as a contraindication to busulphan therapy; the development of thrombocytopenia commonly heralded the onset of the terminal acute phase. Drug toxicity was rare and mainly due to overdosage; pancytopenia was the most ominous of such effects. Resistance to therapy was usually due to the onset of the acute terminal phase—an occurrence to be expected in some 50% of patients whether treated or untreated.

The longest remissions were achieved when the leucocyte count was reduced to 10,000 per c.mm. or less. The median survival time (42 months) in the series was probably at least as great as with other forms of therapy and greater than in Minot's series of untreated cases (31 months).

"Repeated courses of busulphan are considered to offer an effective and practical palliative form of therapy for chronic myelocytic leukaemia, up to the time of appearance of the terminal acute myeloblastic phase."

R. B. Thompson

Respiratory System

396. **The Bacterial Flora of the Nose, Naso-pharynx and Adenoids.** (Sledování bakteriální flóry v nose, v nosohltanu a v adenoidních vegetacích)

Z. HYNKOVÁ. *Československá pediatrie* [Čsl. *Pediat.*] 16, 151-153, Feb., 1961.

An investigation of the bacterial flora of the upper respiratory tract was carried out on 60 children (36 girls, 24 boys) whose average age was about 6 years. The children were in good health at the time, but had been referred for tonsillectomy for such reasons as mouth-breathing while asleep, frequent rhinorrhoea and colds, recurrent otitis, slight deafness, and frequent attacks of tonsillitis.

The bacteriological examination of the nose was carried out with a small, sterile, cotton-wool swab, the specimens being immediately inoculated on to blood-agar. A swab was then taken from the nasopharynx by means of a small, sterile, cotton-wool swab contained within a sterile glass tube, the specimens thus obtained being again inoculated direct on to blood-agar. Finally, a small particle of adenoid tissue was removed for bacteriological investigation. The numbers of cases in which positive cultures were obtained are tabulated:

Organism	Nose		Naso-pharynx		Adenoid Tissue	
	No.	%	No.	%	No.	%
Non-haemolytic <i>Staphylococcus albus</i> ..	50	83.33	53	88.33	52	86.66
α -Haemolytic streptococci ..	23	38.33	58	93.33	59	98.33
Haemolytic <i>Staph. aureus</i> ..	15	25.0	14	23.33	16	26.66
<i>Diplococcus pneumoniae</i> ..	7	11.6	13	21.66	12	20.0
β -Haemolytic streptococci ..	3	5.0	30	50.0	33	55.0
<i>Neisseria catarrhalis</i> ..	2	3.33	4	6.66	4	6.6

From the results of these investigations the author concludes that whereas non-haemolytic *Staph. albus* is the predominant organism in the nose, in the nasopharynx and adenoids it is associated with α -haemolytic streptococci, which in fact predominate there. It is interesting to note that although these bacteria were present in most cases there were no clinical symptoms or pathological signs at the time of testing. He concludes that careful swabbing of the nose and throat is an important procedure when deciding whether tonsillectomy should be performed as in many cases there are no other indications of disease.

Paul Frankl

397. Pulmonary Embolism

P. R. ALLISON, M. S. DUNNILL, and R. MARSHALL. *Thorax* [Thorax] 15, 273-283, Dec., 1960. 13 figs., 4 refs.

In experiments carried out in the Nuffield Department of Surgery, Oxford, the fate of artificial pulmonary emboli was studied in dogs. Radio-opaque thrombi, large in relation to the size of the dogs, were prepared

from the dogs' own blood and introduced into the inferior vena cava or jugular vein. The passage of the clot and its ultimate lodgement in the pulmonary arteries were studied by cine and still radiography. The passage of the clots caused no change in the pulse, systemic blood pressure, or electrocardiogram, but defaecation sometimes occurred. Subsequent radiographic study did not demonstrate any additional opacity in the lung, such as might be produced by an infarct or pleural fluid. The clots shrank markedly during the next few hours. Morbid anatomical studies were made at intervals. On the 4th day there was a smooth layer of cells covering the clot and vasa vasorum, derived from the bronchial arteries, were growing into it from the adventitia. By the 7th day the clot was flattened against the wall and collagen was forming beneath the new "endothelium". At 21 days there was no recognizable clot, but there were several foci of fibrosis, mainly at bifurcations, containing dilated vascular channels—a process of organization rather than canalization. At 28 days these foci had disappeared, leaving apparently normal arteries.

Two case histories of pulmonary embolism in man are given. In the first, ending fatally with a block of the left main pulmonary artery, multiple emboli were given off during the preceding 7 months. In the second emboli were given off during one month and recovery followed embolectomy; it is noteworthy that the emboli were removed with forceps from both pulmonary arteries after suction had yielded nothing but blood.

If the results of the animal experiments are applicable to man it follows that there is no clinical way of diagnosing pulmonary embolism unless it occurs in the presence of previous severe pulmonary arterial obstruction or pulmonary venous congestion. It seems possible that repeated small postoperative embolisms might be a normal and undetectable occurrence and that death might follow a single large embolism when previous small ones were occurring faster than they could be absorbed.

Bernard J. Freedman

398. The Use of Radioactive Carbon Dioxide to Measure Regional Blood Flow in the Lungs of Patients with Pulmonary Disease

J. B. WEST, C. T. DOLLERY, and P. HUGH-JONES. *Journal of Clinical Investigation* [J. clin. Invest.] 40, 1-12, Jan., 1961. 7 figs., 7 refs.

Carbon dioxide labelled with oxygen¹⁵ has been used to measure regional pulmonary blood flow in a series of 30 patients with a variety of lung diseases. The isotope has a half-life of only 2 minutes and is prepared in a cyclotron in the hospital grounds. For the patient, the measurement is very simple and the radiation dose is small. He takes a single breath of air containing a small quantity of active gas and breath-holds for 15 seconds. Scintillation counters placed in front of and behind the chest detect the activity of gas within the lung, and the

clearance rate during breath-holding is a measure of the pulmonary blood flow in the lung core examined.

Good correlation was found between the radioactive measurements and angiograms in 4 patients, but the plain radiographs showed some interesting discrepancies in a further group. In most cases the radioactive carbon dioxide clearance rates were found to be closely related to radioactive oxygen and carbon monoxide clearance rates. Striking increases in local blood flow were found in apparently normal areas in the presence of disease elsewhere in the lung, and this complicates a comparison with clearance rates determined from normal subjects. The use of radioactive carbon dioxide for measuring regional blood flow compares favorably with the traditional techniques of angiography and bronchspirometry. —[Authors' summary.]

399. The Respiratory Effects of Meperidine Alone and in Combination with Levallorphan in Patients with Pulmonary Emphysema

W. U. REIDT, J. H. CULLEN, and L. H. E. SMITH. *American Review of Respiratory Diseases* [Amer. Rev. resp. Dis.] 83, 481-488, April, 1961. 1 fig., 16 refs.

The respiratory effects of meperidine and meperidine in combination with levallorphan were measured in 13 patients with pulmonary emphysema and in 3 patients without pulmonary disease. Levallorphan combined with meperidine in a ratio of 1:60 produced a greater mean increase in arterial carbon dioxide pressure and a greater mean decrease in alveolar ventilation than meperidine alone, whereas a ratio of 1:100 produced less.

Significant respiratory depression occurred in 7 of 8 patients tested with the 1:60 mixture and in 3 of 8 tested with the 1:100 mixture. In none of the patients did the ventilatory values following levallorphan and meperidine in combination equal the control values.

Levallorphan, when used with meperidine in a ratio of 1:100, provided incomplete protection against the respiratory effects of meperidine in some but not all patients. Levallorphan used in combination with a narcotic cannot be relied upon to prevent respiratory depression in patients with pulmonary insufficiency. —[Authors' summary.]

400. Four and One-Half Years' Experience in the Treatment of Emphysema and Other Respiratory Insufficiencies by Tracheal Fenestration

E. E. ROCKEY, C. F. BLAZSIK, S. A. THOMPSON, and S. VIRABUTR. *Diseases of the Chest* [Dis. Chest] 39, 117-128, Feb., 1961. 6 figs., 9 refs.

The operation of tracheal fenestration is designed to create a valvular opening into the trachea through which tracheo-bronchial suction can be carried out over many months, even by the patient himself. From the New York Medical College-Metropolitan Medical Center and St. Anthony's Hospital, Woodhaven, New York, the authors report their experience of this operation in 36 cases treated over the preceding 4½ years. All the patients had evidence of cor pulmonale and 9 of them had heart failure; they therefore represented a severely crippled group. The majority were patients with em-

physema with or without broncho-pulmonary infection. The results have been assessed clinically (facilities for detailed respiratory function studies have only recently become available). There was one operative death; one patient derived no benefit, 14 were "made more comfortable", and 9 were made fit enough to return home, while 11 had progressive improvement sufficient to allow them to lead a reasonable life and some to return to work. However, at the time of review only 14 of the original 36 patients were living, which is an indication of the severity of the underlying condition rather than a reflection on the operation.

The authors underline the point that any benefit is derived solely from suction clearance of the tracheo-bronchial tree; even in the "dry" cases of emphysema this seems to be the essential factor. They strongly recommend the use of special catheters designed to reach the segmental orifices.

W. P. Cleland

INFLAMMATORY DISEASES OF THE LUNG

401. Preliminary Report: Epidemiology of Infections Due to the Atypical Acid-fast Bacilli

E. C. PRATHER, J. O. BOND, E. C. HARTWIG, and F. P. DUNBAR. *Diseases of the Chest* [Dis. Chest] 39, 129-139, Feb., 1961. 2 figs., 12 refs.

The laboratories associated with the Bureau of Preventable Diseases of the Florida State Board of Health, Jacksonville, have identified 585 persons harbouring atypical acid-fast bacilli during a 4-year study. Approximately 75% of the organisms were of the non-photochromogenic type (Group III), 4.9% were photochromogenic mycobacteria (Group I), 12.6% were of the slow-growing scotochromogenic type (Group II), and 9.3% were rapid growers (Group IV). They occurred mainly in older males and showed seasonal variation in incidence, with a geographical distribution according to type. A large proportion of the known cases occurred in rural populations of a low socio-economic class.

Mantoux testing of school-children showed that 6.6% reacted to atypical tuberculin and 1.1% to standard tuberculin. Reactions to the former occurred in 16.4% of coloured as against 3.5% of white children. The coloured race also had a higher attack rate of overt disease. Of 69 children positive to either or both antigens, 2 showed radiological evidence of active primary tuberculosis, of whom one reacted only to the atypical antigen. Skin testing and sputum examination of the contacts of children reacting to either antigen revealed a definite family clustering. In similar investigations, including x-ray examination, of approximately 500 contacts of 80 patients with known pulmonary disease and infection with non-photochromogenic mycobacteria approximately 25% gave a positive reaction to atypical tuberculin, the sputum of 5 (3.8%) yielded non-photochromogenic atypical bacilli, and only 11 (3.4%) had evidence of present or past pulmonary disease.

In only 146 (38%) of 386 cases with adequate records was there evidence of a primary relationship between

the presence of the atypical organism and demonstrable disease. Four of these patients had disease of the kidney due to acid-fast bacilli and 142 had x-ray evidence of pulmonary disease. No apparent abnormality was found in 16 (4%), and 224 (58%) had bacteriological or clinical evidence, or both, of other causes to explain the manifest disease.

B. Golberg

402. Plastic Bronchitis

R. S. JOHNSON and E. G. SITA-LUMSDEN. *Thorax* [Thorax] 15, 325-332, Dec., 1960. 3 figs., 15 refs.

From Southend-on-Sea Hospital, Essex, 4 cases of recurrent plastic bronchitis are reported. All the patients were women, of whom 3 were over 60 years of age. The attacks were of fairly abrupt onset with chest pain, fever, cough, severe dyspnoea, and signs of collapse. The affected bronchi were obstructed by plugs of tough, inspissated mucus, with consequent collapse of distal segments and, in one instance, of an entire lung. The plugs were coughed up or, failing that, removed bronchoscopically and this was followed by prompt recovery. In appearance the casts resembled boiled macaroni, with some branching, and some were several centimetres long. Some casts contained Charcot-Leyden crystals and Curschmann's spirals as well as sundry pathogenic organisms. Bronchoscopic biopsy showed inflammatory changes, with some flattening of the epithelium in one case. The 4 patients had a total of 27 attacks of pulmonary collapse, of which 25 were left-sided. All gave a previous history of recurrent bronchitis.

The literature is reviewed and the aetiology is discussed without, however, a firm conclusion being reached. Apart from infection, allergy is believed to play a part. Although *Aspergillus fumigatus* was grown from the sputum of one patient, she differed from the others in having eosinophilia. Moreover, the casts differed from those of *Aspergillus* infection, which are friable and brownish-yellow.

Bernard J. Freedman

403. Eaton Agent Pneumonia

R. M. CHANOCK, M. A. MUFSON, H. H. BLOOM, W. D. JAMES, H. H. FOX, and J. R. KINGSTON. *Journal of the American Medical Association* [J. Amer. med. Ass.] 175, 213-220, Jan. 21, 1961. 17 refs.

This is a report of an epidemiological study carried out at a U.S. Marine Corps training centre over a period of 6 months, during which time the average recruit strength was 5,000. Of the 238 recruits who developed atypical pneumonia, 161 (68%) showed evidence of infection with Eaton agent as shown by the fluorescent antibody technique of Liu. A rise in antibody titre was also noted in 40 (28%) of 144 recruits suffering from a non-specific respiratory illness. Eaton agent was recovered from 14 of 17 patients with serologically positive pneumonia by culture in monkey kidney tissue.

Eaton agent was widely disseminated throughout the centre; tested at a level of 1 in 10 serum dilution, 17% of recruits were found to be positive on entering the camp, and by the completion of training 44% had become positive. Pneumonia was common, occurring in 2% of recruits, and 1-5% developed Eaton-positive

pneumonia. Only 1 in 30 infections with Eaton agent resulted in clinical pneumonia, and although some non-pneumonic febrile illnesses were attributed to this organism, the majority of infections with Eaton agent appeared to be unassociated with recognized illness.

K. C. Robinson

404. Pneumothorax Accompanying Staphylococcal Pneumonia in Patients Treated with Steroids

K. H. OLESEN and F. QUADE. *Lancet* [Lancet] 1, 535-536, March 11, 1961. 10 refs.

During the 2 years 1958-9 4 patients were seen in the Epidemic Department of Blegdamshospitalet, Copenhagen, in whom staphylococcal pneumonia was complicated by symptomless spontaneous pneumothorax. All the patients had been treated with corticosteroids. Three were female, aged 14, 3½, and 9 years, and were admitted with systemic lupus erythematosus, staphylococcal pneumonia, and acute leukaemia respectively. The one male, aged 23, had acute porphyria. In every instance the pneumothorax was discovered on routine radiography, the radiograph being taken between 11 and 28 days after steroid treatment had begun. Out of 7,517 patients admitted to the department during the same period, 45 had staphylococcal pneumonia, 19 receiving steroids; 4 developed pneumothorax, all having had steroid treatment. Of the remaining 7,472 patients who did not develop staphylococcal pneumonia, 200 received steroids and 7,272 did not. Three patients in each of these groups developed spontaneous pneumothorax.

The figures suggest that pneumothorax is a common complication of staphylococcal pneumonia and that treatment with steroids may increase the liability, although masking the symptoms. It would also appear that treatment of other diseases with steroids may lead to pneumothorax.

Arthur Willcox

405. Current Observations in Pneumococcal Pneumonia: I. Azotemia as a Prognostic Omen

G. E. HORTON, R. D. GOURLEY, R. H. WALKER, and E. ULRICH. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] 241, 322-328, March, 1961. 1 fig., 23 refs.

The clinical notes in all cases of pneumococcal pneumonia treated at the Veterans Administration Medical Teaching Group (Kennedy) Hospital, Memphis, Tennessee, between 1957 and 1959 were reviewed and the relation between the blood urea level and the ultimate fate of the patient studied. All of 7 patients who died had had a high blood urea level on admission which remained so or rose even higher. Of the 96 survivors, 70 had a normal blood urea level (25 mg. per 100 ml. or less) throughout, and in the others a high initial value rapidly fell, with one exception, to normal. From a study of the kidneys post mortem it was concluded that no specific renal lesion was responsible and that the azotaemia could be explained on a pre-renal basis, although it is made worse by pre-existing renal disease. This observation on the prognostic value of the blood urea level in pneumococcal pneumonia does not apply to acute pneumococcal conditions, such as meningitis, without pulmonary involvement.

A. Gordon Beckett

Urogenital System

406. Urinary Tract Infection: a Comparative Study in the Diabetic and General Populations

D. J. O'SULLIVAN, M. G. FITZGERALD, M. J. MEYNELL, and J. M. MALINS. *British Medical Journal [Brit. med. J.]* 1, 786-788, March 18, 1961. 1 fig., 21 refs.

For this study, carried out at Birmingham General Hospital, 150 patients attending the diabetic clinic were selected at random, their age and sex distribution corresponding to that of the clinic population of 3,841 patients; a further 150 matched subjects selected from among minor casualty out-patients were studied as a control. Mid-stream specimens of urine were obtained by standard techniques, plated immediately aerobically, and viable counts performed. Bacterial counts of over 100,000 per ml. of urine were obtained in 20 (13.3%) of the diabetics and in 18 (12%) of the controls; of these 38 patients the great majority (35) were elderly or middle-aged women; 12 of the patients were aged 40 to 59 years, 25 over 60, and only one under 40. Among the organisms isolated *Escherichia coli* predominated, with a few cases showing *Proteus vulgaris*, *Bacillus lactis aerogenes*, or *Streptococcus faecalis*. The only notable difference between the two groups of patients was that of the 20 diabetics with counts over 100,000 per ml. 15 showed a count of more than 1,000,000 per ml., whereas only 7 of the 18 infected controls did so. This was considered to be probably due to the heavy glycosuria in the diabetics encouraging growth in the urine.

Contrary to the previous weight of opinion, therefore, urinary infections are no more common in diabetics than in non-diabetics. It is suggested that failure to take into account the large number of middle-aged and elderly women in the diabetic population has probably led to this erroneous conclusion.

Arnold Pines

407. Response to Bacterial Pyrogen in the Differential Diagnosis of Chronic Urinary Tract Infection

G. PIGEON, M. SAINT-MARTIN, and J. GENEST. *Canadian Medical Association Journal [Canad. med. Ass. J.]* 84, 360-363, Feb. 18, 1961. 11 refs.

In 1959 Pears and Houghton (*Lancet*, 2, 1167; *Abstr. Wld Med.*, 1960, 27, 461) suggested that, in chronic renal infections, the excretion in the urine after the injection of a bacterial pyrogen of more than 100,000 leucocytes and non-squamous cells per hour may be diagnostic. In the present study, reported from the Hôtel-Dieu Hospital, Montreal, 4 patients who were excreting less than 100,000 (from 16,900 to 96,100) cells per hour and who were suspected to be suffering from chronic pyelonephritis were given intravenously 0.007 µg. per kg. body weight of the bacterial pyrogen "lipeal", a purified lipopolysaccharide derived from *Salmonella abortus equi*. In the urine, collected 30 and 60 minutes later, of all 4 patients the cell count rose above 100,000 per hour (from 122,500 to 539,850 (192 to 1,636%) and was considered diagnostic of pyelonephritis. In 5

patients known to have cystitis only there was a decrease in the cell count after an injection of lipeal, though in 4 the initial count had been over 100,000. The authors suggest that this test therefore clearly differentiates between chronic cystitis and pyelonephritis.

Arnold Pines

408. Treatment of Renal Failure in a Unit with Facilities for Haemodialysis (Twin-coil Artificial Kidney): Results with 80 Patients

R. C. JACKSON, N. V. D. BUNKER, W. J. ELDER, and A. M. JOEKES. *British Medical Journal [Brit. med. J.]* 2, 1909-1916, Dec. 31, 1960. 2 figs., 22 refs.

A survey is made of the results of treatment of 80 patients in a unit with haemodialysis facilities during a two-year period; 78 patients were admitted and 88 dialyses performed on 57 of them; a further 2 patients were dialysed successfully once each in their own hospitals.

Acute recoverable renal failure occurred in 36 patients and 27 recovered from their renal failure. Nine further patients in this group, but with associated hepatic lesions, 2 of whom recovered, are discussed separately as the prognosis is thought to depend on the hepatic lesion. Twenty-nine cases of acute irrecoverable renal failure and chronic renal lesions are described and only 4 improved in these two categories. The use of the artificial kidney for barbiturate poisoning is discussed. Emphasis is placed on early diagnosis of renal failure by observations on the urine rather than isolated estimation of the blood chemistry, and treatment is discussed. The clinical state of the patient is the single most important indication for dialysis; other factors are marked hyperkalaemia of 7 mEq. per litre or more, a severe acidosis of 12 mEq. per litre or less, and gross overhydration. A description is given of the technique and results of dialysis.

The results of the present and other series are discussed and two conclusions are drawn: (1) all patients with more than a transient acute renal failure should be transferred to specialized units; and (2) the establishment of specialized units with haemodialysis facilities should be on a planned basis, taking into consideration population densities. Case histories are given of 5 patients who recovered from extensive trauma.—[Authors' summary.]

409. Pulmonary Ventilation (Becklake's Index) in Renal Failure with Special Reference to Overhydrated Patients with "Fluid Lung". [In English]

H. FRITZ and B. LINQVIST. *Acta medica Scandinavica [Acta med. scand.]* 169, 181-191, Feb., 1961. 14 refs.

Overhydration in the presence of acute renal insufficiency may cause pleural effusion or congestive changes which are [neatly] described by the authors as "fluid lung". The radiological picture is characteristic. In

this paper from the University of Lund, Sweden, they report a study of pulmonary ventilation in 65 patients with this syndrome, and in 10 normal subjects. The subjects breathed oxygen and the apparatus recorded instantaneously the nitrogen content of the expired air. This nitrogen elimination technique permitted the calculation of Becklake's index, that is, the amount of pure oxygen in litres which, per litre of functional residual air, is required to lower the nitrogen content in the end-tidal gas from normal values to 2%. This index is therefore increased in patients with patchy or generalized alveolar hypoventilation.

In 60 observations on 10 normal subjects the mean value for Becklake's index was 6.9 ± 0.85 litres, whereas 228 estimations in the 65 patients with renal disease gave a mean of 9.4 litres. The index for 24 renal patients without radiological signs of "fluid lung" or pleural effusion was 8.8 litres, and in 22 with slight, 8 with moderate, and 7 with marked changes it was 9.2, 10.5, and 10.7 litres respectively. Overhydration thus impairs ventilation or renders it uneven, even in the absence of radiological changes in the lungs.

In 9 patients serial studies performed during the correction of overhydration showed a reduction of Becklake's index from a mean of 10.1 to 8.6 litres. In 21 uraemic patients, as pulmonary changes increased or decreased, the index showed the expected parallelism in 16 (78%). The mean index was 9.5 litres in 21 patients with pleural effusion but without "fluid lung", 9.9 in 54 with bronchitis or bronchopneumonia, and 8.0 in 31 uraemic states. The highest values (mean 10.3 litres) were obtained in uraemic patients with bronchitis or bronchopneumonia. The radiological appearances of "fluid lung" also correlated with the measured values for vital capacity, but not with those for tidal air.

T. B. Begg

410. Pyelonephritis: Observations on the Relation between Various Diagnostic Procedures

M. S. R. HUTT, J. A. CHALMERS, J. S. MACDONALD, and H. E. DE WARDENER. *Lancet* [Lancet] 1, 351-357, Feb. 18, 1961. 9 figs., 8 refs.

This paper from St. Thomas's Hospital, London, assesses the value of various diagnostic tests in acute and chronic renal infections and throws some light on the pathological significance of this group of diseases. Of 15 patients with acute pyelitis which had already been treated with antibiotics, renal biopsy examination showed pyelonephritis in as many as 5, although the excretion pyelogram was normal in all but 2. The urinary leucocyte excretion rate was still abnormally high (over 400,000 per hour) in 6 out of 14 patients tested, and this despite a sterile urine in 3 cases, while in 6 out of 13 patients leucocyte excretion was raised to an abnormally high level by the intravenous injection of a bacterial pyrogen ("pyrexal"); a positive result in either test indicates persistent inflammation of the renal tract. The glomerular filtration rate (G.F.R.), measured by the clearance of creatinine, was normal (69 to 113 ml. per minute) in 10 out of 14 cases; in 3 of the 5 cases with biopsy evidence of pyelonephritis the G.F.R. was 50 ml. per minute or less.

Chronic pyelonephritis was diagnosed in 26 patients on the basis either of renal biopsy examination or of recurrent urinary infections together with an abnormal excretion pyelogram. Of 12 patients whose renal biopsy showed chronic pyelonephritis, only 5 gave a history of previous renal infection and 10 had a normal excretion pyelogram, but 11 of the 12 had proteinuria. Of the 26 excretion pyelograms, 7 gave a normal result, 2 showed no shadow, and 17 revealed an abnormal pattern due to cortical thinning, calyceal deformities, or calculi. It is recalled that chronic pyelonephritis is a patchy disorder and the renal biopsy specimen may not happen to include an abnormal area. Of 15 patients treated with antibiotics at least one month previously, 7 still had infected urine, 9 had an abnormally high leucocyte excretion rate (pyuria), and 11 showed pyuria after the injection of the pyrogen. Of 11 patients who had received antibiotics more recently, 2 had infected urine, 6 had pyuria, and only 4 showed normal leucocyte excretion rates after the intravenous pyrogen injection. The diastolic blood pressure was between 95 and 160 mm. Hg in 14 of the 26 patients, and creatinine clearance was low (25 to 60 ml. per minute) in 11.

The over-all conclusion is that chronic pyelonephritis is a disease difficult to diagnose without the aid of several tests, is difficult to eradicate, and is always potentially harmful. It is pointed out that the intravenous injection of the pyrogen induced pyuria in several patients with acute or persistent glomerulonephritis or essential hypertension, so that these diseases must be excluded before a positive result of the pyrogen test is interpreted as an indicator of persistent infective inflammation of the kidneys.

T. B. Begg

411. The Problem of Chronic Primary Interstitial Nephritis. (Le problème de la néphrite interstitielle chronique primitive)

A. LARCAN, G. RAUBER, and C. HURIET. *Presse médicale* [Presse méd.] 69, 652-655, March 22, 1961. 6 figs., 40 refs.

In this paper from the Clinique Médicale, Nancy, the authors discuss the clinical manifestations, natural history, urinary findings, biopsy picture, and aetiology of what the authors call primary chronic interstitial nephritis. A few cases are described (and illustrated by some excellent histological photomicrographs). This condition is a slowly progressive syndrome beginning with vague ill-health and progressing to renal failure in some cases. Bacteriuria is frequent. The renal biopsy picture is patchy and includes the whole range of atrophic, hypertrophic, infiltrative, and vascular changes, so that it is impossible to determine which are the primary changes.

The authors suggest that various factors, including chronic intoxications (for example, with phenacetin), nutritional and metabolic disorders, and repeated infection, may all contribute to the causation.

[This syndrome would be accepted as chronic pyelonephritis by many urologists; some cases may be examples of chronic glomerulonephritis.]

T. B. Begg

Endocrinology

412. Effect of Parathyroidectomy on the Incidence of Renal Calculi

M. G. McGEOWN. *Lancet [Lancet]* 1, 586-587, March 18, 1961. 3 refs.

In 56 patients with hyperparathyroidism treated at Belfast City Hospital the author has compared the rates of formation of renal stones before and after parathyroidectomy.

It was found that during 401 patient-years before the operation 99 stones formed after the first ones had been detected, whereas in 158 patient-years after the operation only 8 stones formed or enlarged. The preoperative rate of stone formation was calculated for each patient by dividing the number of stones formed by the number of years since the recognition of the first stone. If each patient had continued developing stones at the same rate the number of stones expected in successive years after operation would have been approximately 19, 19, 12.6, 11, and 9 respectively, whereas the actual numbers observed in the 5 postoperative years were 3, 2, 1, and 0. Both methods of analysis show a very significant reduction ($P < 0.001$) in the rate of formation of renal calculi after parathyroidectomy. Since the incidence of renal calculi in hyperparathyroid patients is at least 22% it is suggested that all patients with renal calculi should be investigated for possible hyperparathyroidism.

G. C. R. Morris

THYROID GLAND

413. The Electroencephalogram in Congenital Hypothyroidism: a Study of 10 Cases

E. A. NIEMAN. *Journal of Neurology, Neurosurgery and Psychiatry [J. Neurol. Neurosurg. Psychiat.]* 24, 50-57, Feb., 1961. 3 figs., 17 refs.

It has been observed that although a proportion of cretins show satisfactory somatic improvement in response to treatment, they fail to make adequate mental progress and remain severely retarded. This paper from the Royal Southern Hospital, Liverpool, records the electroencephalographic (EEG) changes in 10 patients with hypothyroidism. In 3 of these who were aged under 6 months the records showed a remarkable absence of artefacts—owing perhaps to the lack of spontaneous movement in these infants—and an unusually regular theta activity, while they surprisingly presented an appearance of unusual maturity, which the author attributes to mental torpor; the recording became more dysrhythmic with treatment. A further 4 patients were aged between 4 and 9 years; they had been inadequately treated, but nevertheless made fair progress with proper dosage of thyroid extract. Of 2 children who did badly the EEG was abnormal in one and normal in the other. The remaining case was that of a woman aged 33 who

had been treated in infancy but allowed to lapse into myxoedema when adult. The EEG in this case was normal, probably because of adequate treatment in earlier life.

The author suggests that myxoedematous patients who fail to develop mentally despite treatment with thyroid extract usually have abnormal EEG records and that the most likely explanation of the mental retardation is an associated cerebral dysgenesis. Brief histories of the 10 patients are given and illustrative EEG recordings are reproduced.

N. S. Alcock

414. Pulmonary Function in Hyperthyroidism

M. STEIN, P. KIMBEL, and R. L. JOHNSON JR. *Journal of Clinical Investigation [J. clin. Invest.]* 40, 348-363, Feb., 1961. 8 figs., bibliography.

In this paper from the Graduate School of Medicine, University of Pennsylvania, Philadelphia, the authors describe an attempt to correlate the dyspnoea which is described in patients with hyperthyroidism with the results of various tests of pulmonary function. The diagnosis of hyperthyroidism was based not only upon clinical assessment, but also upon estimation of the basal metabolic rate, studies of radioactive iodine (^{131}I) uptake, and determination of the serum protein-bound iodine level.

Of the 13 patients, 12 were female; the average age was 41 years. Nine patients complained of decreased exercise tolerance, 4 mentioning an "inability to get enough air" and 5 having shortness of breath on mild exertion. One patient had had an episode of acute pulmonary oedema one month before the study, but was now fully recovered without antithyroid treatment. One other patient had been in congestive cardiac failure, but was not in failure at the time the various observations were made. No patient had any evidence of tracheal compression from an enlarged thyroid gland. A control group of 6 female euthyroid patients of similar age and body size were also studied.

The vital capacity was decreased in 3 patients, but no correlation was found between the vital capacity, residual volume, functional residual capacity, or total lung capacity at rest and the dyspnoea observed on exercise. The vital capacity was increased in the 7 patients who were studied after treatment for thyrotoxicosis. Maximum breathing capacity was less than 80% of predicted values in 3 patients and lung compliance was lower than the predicted value in "practically all the patients", but the latter increased to normal after treatment. There was an elevation of airway resistance in one patient with a large goitre, but this was insufficient to cause respiratory obstruction. Maximum pressures on inspiration and expiration against a closed airway as measured at the mouth were decreased significantly compared with those in the control group. After treatment these values

increased significantly and it is thought that a weakness of the respiratory muscles is present in patients with thyrotoxicosis. Frequency of breathing at rest was increased in the group and all patients had an increased minute ventilation per unit of body surface area. On exercise ventilation was increased in excess of the oxygen uptake. It appeared that a relationship existed between this finding and the increase in the dead-space ventilation from the tachypnoea and alveolar dead-space ventilation. All these values became normal after antithyroid treatment.

During exercise tests 4 of the hyperthyroid patients complained of dyspnoea which disappeared when the inspired gas was changed from air to oxygen and there was an accompanying fall in the respiratory rate. The pulmonary capillary blood flow was elevated in all the hyperthyroid patients at rest to a level as high as that observed in normal subjects after exercise. However, this elevation was not accompanied by alterations in the pulmonary capillary blood volume, in the membrane diffusing capacity, or in the apparent diffusing capacity of the lung. After treatment the pulmonary capillary blood flow decreased, but the other indices remained unchanged.

J. Warwick Buckler

415. Association of Thyrotoxicosis and Auto-immune Thyroiditis

W. W. BUCHANAN, W. D. ALEXANDER, J. CROOKS, D. A. KOUTRAS, E. J. WAYNE, J. R. ANDERSON, and R. B. GOUDIE. *British Medical Journal* [Brit. med. J.] 1, 843-847, March 25, 1961. 3 figs., 20 refs.

It is the routine practice at the Western Infirmary, Glasgow, to examine the serum of all patients with thyroid disease for the presence of thyroid autoantibodies. As a result two unusual groups of patients have been identified. The first group consisted of 5 patients who were found to be suffering from coincidental hyperthyroidism and autoimmune thyroiditis. In each case the clinical impression of thyroid overactivity was confirmed by an unequivocally hyperthyroid "clinical diagnostic index", as described by Crooks *et al.* (*Quart. J. Med.*, 1959, 28, 211; *Abstr. Wld Med.*, 1959, 26, 300), by ^{131}I -uptake tests, and by measurement of the basal metabolic rate and/or the serum protein-bound iodine (P.B.I.) level. All patients showed positive precipitin tests and strongly positive complement fixation reactions for thyroid autoantibodies, while 3 of them had exophthalmos. Remission of symptoms was produced in all 5 cases by one of the standard methods of treatment of hyperthyroidism. Later thyroidectomy was performed on 3 of these patients and the excised glands showed histological changes of both chronic thyroiditis and hyperthyroidism. Some possible causes of this association are discussed. In 2 of these 5 patients hypothyroidism developed with unexpected rapidity after operation. The susceptibility to postoperative hypothyroidism of thyrotoxic patients whose glands show heavy lymphocytic infiltration has been reported previously. The authors therefore suggest that for thyrotoxic patients in whom precipitin tests are positive non-surgical forms of treatment are more suitable.

The second group, also containing 5 cases, consisted of patients who were at first suspected clinically of having hyperthyroidism. Their response to simple radioactive iodine tests was compatible with this diagnosis, but they were found on subsequent study to have autoimmune thyroiditis. Hyperthyroidism was finally excluded by the demonstration of normal serum P.B.I. levels and of normal suppression of uptake of ^{131}I by the thyroid gland after the administration of thyroxine for 3 weeks. The additional diagnosis was also disproved by the subsequent clinical history, which included a reduction in the size of the goitre after treatment with thyroxine. To avoid misdiagnosis it is suggested that the thyroxine suppression test or the estimation of the serum P.B.I. level should be carried out in all equivocal cases. If this is not possible then the performance of a precipitin test for autoantibodies or, at least, one of the empiric serum flocculation tests is advisable.

H.-J. B. Galbraith

416. Relation of Eye Signs in Graves' Disease to Circulating Antibodies to Thyroglobulin

I. B. HALES, J. MYHILL, F. F. RUNDLE, I. R. MACKAY, and B. PERRY. *Lancet* [Lancet] 1, 468-469, March 4, 1961. 12 refs.

The serum of 98 patients with at least 2 of the 3 classic signs of Graves's disease (exophthalmos, goitre, and hyperthyroidism) was examined at the Royal Melbourne Hospital and the Royal North Shore Hospital, Sydney, by the tanned erythrocyte haemagglutination technique for the presence of antibodies to thyroglobulin. Titres of 1:100 or higher were found in 44% of the patients. Such positive results were obtained in 27 (66%) (including 6 patients with recently developed ophthalmoplegia) of the 41 patients with indubitable exophthalmos, in 4 (17%) of the 23 with lid lag as the only ocular sign, and in 12 (35%) of 34 hyperthyroid patients without eye signs.

It is considered that these findings suggest an association between the form of Graves's disease in which exophthalmos and ophthalmoplegia occur and autoimmune reactions such as are seen in Hashimoto's disease. The authors also point out that lymphocytic infiltration, which is a characteristic feature of the thyroid histology in the latter condition, is also seen in more limited form in the thyroid gland of patients with hyperthyroidism and in the external ocular muscles of those with exophthalmic goitre.

H.-J. B. Galbraith

417. Lymphadenoid Goitre and the Syndrome of Systemic Lupus Erythematosus

R. G. WHITE, B. H. BASS, and E. WILLIAMS. *Lancet* [Lancet] 1, 368-373, Feb. 18, 1961. 4 figs., 22 refs.

The authors, at the London Hospital, have investigated the presence of antinuclear factor in the serum of 40 patients with lymphadenoid goitre, using a histological technique with a fluorescent antibody. In 28 of these patients the diagnosis had been confirmed by histological examination of the thyroid gland. Positive control sera were obtained from cases of systemic lupus erythematosus and negative controls from an antenatal clinic and from routine blood donors. Other tests performed were

complement fixation and precipitin tests and haemagglutination of tanned sheep erythrocytes sensitized with purified thyroglobulin.

Of the 40 cases, 5 gave a positive result for antinuclear factor; all 5 cases were in females aged from 48 to 82 years. In 2 of the cases no other disease was present; one had signs of systemic lupus erythematosus (S.L.E.) 2 years after a positive serum reaction for antinuclear factor had been elicited, while in another case there were features suggesting this disease; and one had rheumatoid arthritis and rheumatic heart disease.

It is suggested that, while these findings are not regarded as supporting the idea that lymphadenoid goitre is a direct manifestation of S.L.E., they may indicate that a small subgroup of cases of lymphadenoid goitre arises in patients with S.L.E. who have a special propensity to form antibodies generally.

B. M. Ansell

418. Myxedema Neuropathy and Myopathy: a Clinical and Pathological Study

S. N. NICKEL, B. FRAME, J. BEBIN, W. W. TOURTELLOTT, J. A. PARKER, and B. R. HUGHES. *Neurology [Neurology (Minneapolis)]* 11, 125-137, Feb., 1961. 2 figs., 27 refs.

At the Henry Ford Hospital, Detroit, and the University of Michigan Hospital, Ann Arbor, the authors studied 25 myxoedematous patients to gain additional evidence of the presence of peripheral neuropathy in myxoedema. All the patients had subjective weakness and tingling, 23 numbness, and 21 impaired memory, while 17 complained of ataxia, 14 of cramps, 15 of tinnitus, and 3 of minor visual hallucinations. Fifteen had peripheral sensory impairment, 7 objective weakness, mainly of proximal muscles, 24 prolonged relaxation of the deep tendon reflexes, 18 dysarthria, 15 mental retardation, 8 the muscle mounding phenomenon, 6 objective ataxia, 5 a positive Romberg's sign, 3 psychosis, and 2 nystagmus, while one patient was in coma with absent reflexes. The peripheral nerves were examined histologically in 12 cases and specimens of muscle in 9.

The endo- and perineurium of most nerves were infiltrated by basophilic material showing metachromasia. Degenerative changes in the myelin sheaths and axis cylinders were present in 3 cases. Normal and abnormal areas appeared in the same microscopical section in 5. Mucoid material in the connective tissue around the nerves was the only abnormality found in 2 cases. Metachromasia of the sarcoplasm and the surrounding connective tissue was present in all the muscle biopsies. Cloudiness, granular appearance, and loss of striations of the myofibrils was found in 4 cases, the changes being mainly confined to larger fibres (90 to 100 μ). Alterations in the number and position of sarcolemmal nuclei were present in 3. Prominent nucleoli were present occasionally. Some muscle fibres showed basophilism of sarcoplasm, endomysium, and perimysium. Mucicarmine stain gave slightly positive results in 3 cases and periodic-acid-Schiff-positive granules were found in 4. The infiltration of peripheral nerves with mucinous material, which could interfere with neuronal metabolism, may account for the sensory abnormalities and part of the weakness. It is suggested that infiltration of

cutaneous sensory corpuscles by a similar substance could be partly responsible for the sensory abnormalities. The reflex changes, muscle mounding phenomenon, and cramps are thought to be due to interference with the contractile mechanism of muscle. The histological findings and distribution of muscle weakness suggest a myopathy. Electromyographic studies showed low potential and also a reduction in the number of motor discharges.

Total serum protein and serum glycoprotein values did not differ significantly from those of controls. The serum levels of γ and β globulins were elevated, whereas that of albumin was decreased. The total serum lipid content was increased, that of the α -lipoprotein fraction being elevated and that of the β -lipoprotein fraction decreased. The levels of the other lipoprotein fractions did not differ significantly from those of controls. The increase in the γ -globulin content of the serum is thought to be due to the presence either of anti-thyroid antibodies or of antibodies against the basophilic substance found in nerves and muscles. The total protein and γ -globulin concentrations in the cerebrospinal fluid (C.S.F.) were significantly increased. The percentage increase in the γ -globulin fraction was statistically significant when γ globulin was determined immunochemically. The increase in total C.S.F. protein might be due to increased permeability at the blood-C.S.F. barrier or to impaired absorption of protein at the arachnoid villi. An antibody response in the subarachnoid villi is postulated as the explanation of the percentage elevation of the C.S.F. γ -globulin content.

There was no correlation between the C.S.F. protein changes, histological findings in muscles and nerves, and the degree of neurological involvement. The terms "myxoedema neuropathy" and "myxoedema myopathy" are suggested for these conditions.

H. S. Schutta

DIABETES

419. Stimulation of the Insular Tissue of the Pancreas by Small Doses of Alloxan. (Стимуляция инсулярной ткани поджелудочной железы малыми дозами аллоксана)

N. A. NAUMOVA. *Проблемы Эндокринологии и Гормонотерапии [Probl. Endokr. Gormonoter.]* 7, 53-56, Jan.-Feb., 1961. 3 figs., 8 refs.

To confirm that small doses of alloxan stimulate hypertrophy of the insular tissue of the pancreas 10 rats were given small doses of alloxan (10 mg. in 0.2 ml. of water) daily for 2 weeks, while another 10 which served as controls were given only 0.2 ml. of physiological saline. Three days after the last injection they were killed under ether narcosis (to prevent any effects from agonal changes in the tissues), the pancreas removed immediately, 40 sections prepared from different regions of each gland, and the number and area of the islets measured.

In the control group a total of 788 islets were found in the 40 sections, with a total area of insular tissue of 7.68

sq.mm., whereas in the 10 alloxan-treated animals there were 1,152 islets, with a total area of 12.6 sq.mm. In the latter group there was thus an increase of 46.2% in the number of islets and one of 64% in the total area. Giant islets (that is, those measuring 45,000 to 78,000 sq. μ) were found 6 times in the control preparations, but 20 times in the treated animals. The β cells were also larger and more numerous in the treated group than in the controls.

In a further study blood sugar curves determined in 3 mice before and after administration of alloxan showed a reduction in the blood glucose level, the average figures being 123, 134, and 124 mg. per 100 ml. respectively before treatment, and 99, 90, and 114 mg. per 100 ml. respectively after alloxan. These findings strongly suggest that small doses of alloxan stimulate hypertrophy of the islet tissue of the pancreas and cause increased functional activity.

L. Firman-Edwards

420. The Gastric Mucosa in Diabetes Mellitus: a Functional and Histopathological Study. [In English]

L. ANGERVALL, G. DOTEVALL, and K. E. LEHMANN. *Acta medica Scandinavica* [*Acta med. scand.*] **169**, 339-349, March, 1961. 6 figs., 33 refs.

Using the augmented histamine test, one of the authors investigated gastric secretion in 56 diabetics admitted to Sahlgren's Hospital, Göteborg, Sweden. Of these, 18 showed absence or marked diminution of gastric secretion, and this paper gives the results of further detailed studies on 10 of these patients. The methods employed included estimation of the uropepsin excretion in 24 hours and of the serum level of cyanocobalamin, the Schilling test (which was repeated after the administration of intrinsic factor in patients showing impairment), estimation of serum iron, examination of bone marrow, and gastric biopsy. For comparison similar investigations were carried out on 5 diabetics with normal acid secretion.

All the cases with achlorhydria or hypochlorhydria showed chronic atrophic gastritis on biopsy; 3 of them appeared to be cases of pernicious anaemia, with a low serum cyanocobalamin level, impaired response to the Schilling test correctable with intrinsic factor, and in 2 cases a megaloblastic marrow. The serum content of iron was low in all cases. The uropepsin output was more variable; the general level in patients with depressed or absent gastric secretion was lower than in those with normal secretion, but there was some overlap between the 2 groups.

The histological findings were those of typical atrophic gastritis with well marked atrophy and varying degrees of inflammation, both superficial and deep. The parietal cells were either absent or grossly reduced in numbers, and there was intestinal metaplasia in all except one case. The only histological change shown in the control group with normal gastric secretion was some mild superficial inflammation. In all cases with chronic atrophic gastritis there were pathological changes in the blood vessels of the tunica mucosae, with hyalinization of the capillaries, which usually stained with periodic-acid-Schiff. It is suggested that these vascular changes may be the

result of a nutritional disturbance and may themselves be a contributing factor in the development of the chronic atrophic gastritis.

T. D. Kellock

421. Tolbutamide Tolerance Test in Carbohydrate Metabolism Evaluation

N. M. KAPLAN. *Archives of Internal Medicine* [*Arch. intern. Med.*] **107**, 212-224, Feb., 1961. 5 figs., 41 refs.

The author has compared the clinical usefulness of a tolbutamide tolerance test with that of a glucose tolerance test in 456 patients at the U.S.A.F. Hospital, Lackland Air Force Base, Texas. In the former, which was shown to have excellent reproducibility, blood sugar levels were measured 20, 30, and 60 minutes after the intravenous injection of 1 g. of tolbutamide.

In non-diabetic patients (105) the blood sugar level fell to 80% or less (mean 65%) of the fasting level at 20 minutes and to 77% or less (mean 57%) of the fasting value at 30 minutes. All of the overt diabetics (55), with fasting hyperglycaemia, had a smaller and less rapid fall in blood sugar level; none were below 84% at 20 minutes (mean 94%) or below 77% at 30 minutes (mean 90%). The milder the diabetes, the greater the fall in blood sugar level.

Of the 73 patients with abnormal glucose tolerance but normal fasting levels, 22 showed a normal fall and return to normal after tolbutamide; in 16 of these given a repeat test after one year the results were the same. Of the 17 patients in this group with a family history of diabetes, 15 gave an abnormal response to the tolbutamide test.

Of 44 patients with normal glucose tolerance and a family history of diabetes, 12 had an abnormal curve after cortisone provocation. All 12 patients gave a normal response to tolbutamide, but 2 of the others showed a slightly diminished response.

Among the 15 patients over the age of 60, 8 had abnormal glucose tolerance, but only 3 responded abnormally to the tolbutamide test. Similarly, of the 23 obese patients, 14 had abnormal glucose tolerance, but only 3 showed a decreased tolbutamide response. All 3 patients had a positive family history of diabetes, whereas only 3 others among the entire group had such a history. Of the 26 with abnormal glucose tolerance among 39 patients with liver disease, only 14 gave an abnormal response to tolbutamide injection. Similarly, of the 15 patients given steroids and the 16 with thyrotoxicosis, only half of those with abnormal glucose tolerance displayed diminished responsiveness to tolbutamide.

In pregnancy (71 cases), however, the response to tolbutamide decreased as the pregnancy progressed, but these abnormal responses did not appear to have any prognostic value. Therefore it is recommended that the result of the test in pregnancy should be interpreted very cautiously.

The author believes that the tolbutamide test shows an improved specificity for diabetes over the glucose tolerance test, only half of those with abnormal glucose tolerance giving a positive response to the tolbutamide test. He finds support for this view in the fact that other studies suggest that many subjects with abnormal glucose

tolerance are not diabetic, the carbohydrate tolerance returning to normal after a time. He considers that further follow-up of these patients is desirable.

A. Gordon Beckett

422. The Effect of Prednisolone on Glucose Tolerance in Respect to Age and Family History of Diabetes Mellitus
M. J. SANDERS. *Diabetes [Diabetes]* 10, 41-45, Jan.-Feb., 1961. 6 figs., 18 refs.

In this study of the effect of prednisolone on glucose tolerance, carried out at the Alfred Hospital, Melbourne, 77 persons in all were investigated, these being divided into three groups: (1) 16 subjects with a family history of diabetes and 14 controls with no such history, all under 20; (2) 18 subjects with a family history of the disease and 12 controls, all aged between 20 and 40; and (3) 8 relatives of diabetics and 9 controls, all aged over 40. Two glucose tolerance tests were performed, the second being preceded by 1 mg. of prednisolone per 14 lb. (6.35 kg.) body weight given 12 hours and again 2 hours before the test.

The results confirmed that the relatives of diabetics in all age groups showed a greater decrease in carbohydrate tolerance after prednisolone compared with the controls. There was also a loss of glucose tolerance with increasing age in both the relatives of diabetics and in the control subjects. It is noted that the decrease of carbohydrate tolerance was mainly shown in the second hour of the test.

In conclusion the author states that only a long-term follow-up will show whether relatives of diabetics giving a negative response to this prednisolone-augmented test are less prone to develop diabetes than those giving a positive response. The status of the prednisolone test is still uncertain as a means of detecting a pre-diabetic state, but in the author's view it appears to be reliable in patients up to the age of 40. Full detailed results are presented in graphs and tables.

I. McLean Baird

ADRENAL GLANDS

423. Reduction of Adrenal-steroid Production by an Inhibitor of Cholesterol Biosynthesis

J. C. MELBY, M. ST. CYR, and S. L. DALE. *New England Journal of Medicine [New Engl. J. Med.]* 264, 583-587, March 23, 1961. 6 figs., 13 refs.

In the study here reported from the University of Arkansas Medical Center, Little Rock, triparanol, an efficient inhibitor of cholesterol synthesis, was given to 7 healthy subjects and 2 patients with hyperadrenalism and found to reduce significantly the production of cortisone and aldosterone. The drug was given by mouth in doses of 500 mg. twice daily. The urinary excretion levels of 17-hydroxycorticosteroids, 17-ketogenic steroids, 17-ketosteroids, and the tetrahydrometabolite of aldosterone were determined by methods described. Adrenal stimulation was carried out by injections of 80 units of zinc-ACTH intramuscularly twice a day on consecutive days, both before and after the administration of tri-

paranol for 10 days. Recovery of adrenal responsiveness to ACTH stimulation, as reflected by the urinary 17-hydroxycorticosteroid excretion level, occurred within 4 weeks of the discontinuance of triparanol.

In the 2 patients with hyperadrenalism treatment with triparanol strikingly reduced the abnormal excretion of adrenal steroid hormone metabolites, and one of these patients markedly improved clinically during this therapy. No evidence of toxicity was apparent in these experiments, but, as the authors suggest, more extensive studies of this inhibitor of cholesterol synthesis need to be carried out.

G. B. West

424. The Metabolic Effects of Aldosterone Given by Mouth

J. G. G. LEDINGHAM, F. I. R. MARTIN, A. MOXHAM, R. HURTER, and J. D. N. NABARRO. *Lancet [Lancet]* 1, 630-632, March 25, 1961. 5 figs., 4 refs.

From the Middlesex Hospital, London, the authors describe an investigation into the effectiveness of aldosterone (b-aldosterone and its monoacetate) in maintaining sodium balance in patients with Addison's disease or following total adrenalectomy, for which the usual replacement therapy consists in administration of cortisone acetate and 9 α -fluorohydrocortisone (fludrocortisone). Their experiments were carried out on an adrenalectomized dog, one normal man, and 2 women who had undergone total adrenalectomy. Urinary sodium, potassium, and steroid excretion levels were determined by standard methods, while urinary aldosterone content was measured by the method of Ayres *et al.* (*Biochem. J.*, 1957, 65, 639).

The dog was kept on a constant sodium and potassium intake and urinary sodium and potassium excretion measured during short periods of administration of aldosterone intravenously and by mouth and also of fludrocortisone by mouth and compared with a control period during which no steroids were given. Intravenous aldosterone caused marked decrease in the sodium and potassium output, but aldosterone by mouth was much less effective than fludrocortisone; evidently very little steroid given by this route reaches the kidneys in a physiologically active form.

Oral administration of aldosterone to the normal man, who was maintained on a constant diet, was followed by a slight reduction in sodium output. Most of the steroid was excreted as the inactive acid-hydrolysable conjugate. A large dose of the aldosterone monoacetate caused sodium retention and was not excreted as the conjugate. The 2 female patients were maintained on prednisone or cortisone in conjunction with fludrocortisone. It was found that aldosterone by mouth could be used in place of fludrocortisone, but that larger doses (3 mg. per day of aldosterone monoacetate compared with 0.1 mg. of fludrocortisone) were required to maintain sodium balance.

The authors conclude that aldosterone is unlikely to take the place of fludrocortisone in replacement therapy of adrenalectomized patients or those with Addison's disease.

Nancy Gough

The Rheumatic Diseases

425. A Limited Clinical Evaluation of an Egg Yolk Fraction in the Prevention of Rheumatic Recurrences

A. F. COBURN and H. RICH. *A.I.R. Archives of Inter-american Rheumatology* [A.I.R. (Rio de J.)] 3, 498-515, Dec., 1960 [received March, 1961]. 24 refs.

There is circumstantial evidence that improved diet, particularly an increase in the number of eggs consumed, lowers the incidence of attacks of rheumatic fever, and in animal experiments N-(2-hydroxyethyl)-palmitamide (HEP), a fraction of egg yolk, has been shown to have anti-allergic properties in guinea-pigs. The study reported in this paper from New York Medical College was undertaken to determine if HEP could protect susceptible children against recurrent attacks of rheumatic fever and was carried out on 95 children from indigent New York families who had previously been in-patients for rheumatic fever, 152 siblings serving as controls. No antibacterial chemoprophylaxis was given to the patients. It had been previously estimated (from the known recurrence rate of rheumatic fever) that this number of subjects would be sufficient to detect a protective effect of HEP. A placebo-controlled double-blind study was set up and arrangements made for periodic supervision, throat swabbing, and estimation of antistreptolysin-O titres.

In the event, no firm conclusions could be drawn from the study because the expected number of recurrences among the controls did not occur. The authors cite evidence for a considerable improvement in the diet of their subjects (including an increased consumption of eggs) during the period of observation, which may have interfered with the conditions of the study as originally planned. Despite the fact that nearly all subjects developed Group-A streptococcal infections at some time, only 7 recurrences of rheumatic fever were seen, and only one (which occurred a few weeks after starting treatment) was in the HEP-treated group. Although the results of this investigation failed to reach significance at the 5% level, they are nevertheless regarded as promising.

Allan St. J. Dixon

426. Serological Investigations Into Sequelae of Scarlet Fever with Particular Reference to Rheumatic Fever

N. POPOV. *Archives of Disease in Childhood* [Arch. Dis. Childh.] 36, 77-81, Feb., 1961. 2 figs., 13 refs.

The study herein reported is based on the results of detailed clinical and serological studies in 31 children treated at the Second City Children's Hospital, Sofia, Bulgaria, for scarlet fever and followed up for more than 2 years. The serological factors studied included the response to the C-reactive protein test, the erythrocyte sedimentation rate, the plasma fibrinogen level, and the titres of antistreptolysin (ASO) and heterophil agglutinins. Evidence of autoimmunization was sought for in the response to the Coombs test and the antihuman globulin

consumption test of Steffen and in the Rose-Waaler reaction.

Although there was a remarkably high incidence of complications, such as recurrent sore throat and otitis media in 21 of the children, rheumatic fever did not develop in any of the patients. There was no instance of dysproteinaemia, of hyperfibrinogenaemia, or of an extremely high ASO titre, changes which the author accepts as characteristic of rheumatic fever. He therefore concluded that there "was no ground for considering that the post-scarlet fever period was immunobiologically identical with the acute phase of rheumatic fever".

L. E. Glynn

RHEUMATOID ARTHRITIS

427. Rheumatoid Factor and the Pathogenesis of Rheumatoid Arthritis

R. C. MELLORS, A. NOWOSLAWSKI, L. KORNGOLD, and B. L. SENGSON. *Journal of Experimental Medicine* [J. exp. Med.] 113, 475-484, Feb. 1, 1961. 24 figs., 21 refs.

The authors have previously shown (*J. exp. Med.*, 1959, 110, 875; *Abstr. Wld Med.*, 1960, 28, 54) that a fluorescein-labelled aggregated human gamma globulin (F.A.A.G.) was a sensitive reactant for the detection of the 19S macroglobulin complex known as "rheumatoid factor" in preparations of cells and tissue sections. This further report from the Hospital for Special Surgery, New York, describes similar observations utilizing another fluorescent immune complex (F.I.C.) (rabbit antibody to bovine albumin). In this test 127 specimens of synovial and lymph-node tissue from 9 cases of rheumatoid arthritis and 85 from 12 control patients without rheumatoid arthritis were subjected to examination. The specificity of the fluorescent staining attributable to the rheumatoid factor was confirmed by inhibition of the reaction by previous exposure to similar complexes without the labelled fluorescein element.

It was shown that a small proportion of the cells in the richly cellular inflammatory exudate stained with F.I.C., these being plasma cells, both immature and mature and also those of the Russell-body type. (A greater number of cells stained with F.A.A.G., however, than with the F.I.C.) Similar differentiation was obtained by variation of the inhibiting reagents. Two categories of cells in lymph nodes were found to contain rheumatoid factor detectable with F.I.C., namely, the germinal centre cells and the plasma cells; the former may be numerous in hyperplastic lymph nodes. None of the control specimens showed positive staining with the single exception of a specimen from a patient with Waldenström's macroglobulinaemia, which reacted positively with F.A.A.G. and with a fluorescent antibody

for macroglobulin, but did not react with F.I.C. It is concluded that while there is much that is consistent with the hypothesis of the rheumatoid factor being an antibody directed to an altered human gamma globulin and cross-reacting with rabbit gamma globulin, the authors suggest an alternative explanation, namely, that there may be several rheumatoid factors directed against different antigenic components of aggregated human gamma globulin, some of which are present also in the rabbit F.I.C. In an addendum to this paper they announce the preparation of fluorescent reactants in contrasting colours by means of which differential staining of plasma cells can be produced, thus supporting at least a dual nature of cellular rheumatoid factor. *Harry Coke*

428. Electromyographic Changes in Rheumatoid Arthritis

V. L. STEINBERG and C. B. WYNN PARRY. *British Medical Journal* [Brit. med. J.] 1, 630-632, March 4, 1961. 19 refs.

This study was carried out at the Department of Physical Medicine, the London Hospital, on 93 patients with definite rheumatoid arthritis to determine whether electrodiagnostic investigations would throw any light on the cause of the muscular wasting which occurs in this condition. The disease activity was classified according to the method of Duthie *et al.* (*Ann. rheum. Dis.*, 1955, 14, 133; *Abstr. Wld Med.*, 1956, 19, 64). The activity and range of movement of the neighbouring joint was noted, together with the degree of wasting and the power of the selected muscles, these being the small muscles of the hand, the deltoid, the biceps, and quadriceps. Intensity-duration curves were plotted for each muscle, an R.A.F. constant voltage stimulator being used, and electromyography, employing concentric needle electrodes and a GHS double-beam electromyograph, was then carried out on the same muscle. The electromyogram (EMG) was thought to give the most sensitive result, 79 (85%) of the patients showing electromyographic evidence of polymyositis in one or more muscles. The intensity-duration curves revealed partial denervation in 37 of the muscles showing electromyographic evidence of polymyositis and in 2 muscles with a normal EMG.

The authors discuss their findings in relation to previous work on biopsy specimens of wasted muscle in rheumatoid arthritis. They conclude that the changes are not caused by steroid therapy, that there is no constant relationship to wasting and weakness of the muscles and activity of the neighbouring joints, but that there is some relationship between the degree of disease activity and the present findings. *Kenneth Tyler*

429. Prevalence of Rheumatoid Arthritis

J. S. LAWRENCE. *Annals of the Rheumatic Diseases* [Ann. rheum. Dis.] 20, 11-17, March, 1961. 1 fig., 9 refs.

To determine the prevalence of rheumatoid arthritis the author has investigated 2 population samples in the North of England, adapting the criteria recommended by the American Rheumatism Association in 1956 in classifying rheumatoid arthritis as "definite", "prob-

able", and "possible". The 2 areas surveyed were Leigh, Lancashire (751 males, 814 females), and Wensleydale, Yorkshire (485 males, 540 females).

The disease was found to increase in prevalence with age, but tended to appear earlier in males. The minimum prevalence of "definite" disease was 0.4% in males and 1.4% in females; that of "probable" disease 1.7% in males and 3.8% in females. The proportion of positive reactions to the sheep-cell agglutination test (both areas combined) was 4% in males and 5% in females, but positive results were obtained in 67% of the "definite" cases. On the other hand the incidence of positive results in patients with "possible" disease was no greater than in those with "no disease". Of the 1,042 males and 1,157 females examined radiologically, evidence of erosive arthritis, most commonly in the cervical spine, was found in 8%.

Although the clinical grading in the present survey differed in some respects from that of the American Rheumatism Association, there was considerable agreement in regard to the prevalence of rheumatoid arthritis. Applying the findings to the general population of Great Britain, it would appear that at least 377,000 males and 1,034,000 females had "probable" or "definite" rheumatoid arthritis in 1959. *D. Preiskel*

430. Chloroquine Diphosphate in Rheumatoid Arthritis: a Controlled Trial

A. J. POPERT, K. A. E. MEIJERS, J. SHARP, and F. BIER. *Annals of the Rheumatic Diseases* [Ann. rheum. Dis.] 20, 18-35, March, 1961. 6 figs., 26 refs.

In a study at the Rheumatism Research Centre, Manchester University, the value of treatment with chloroquine was assessed in 134 patients, of whom 126 were classified as having "definite" and 8 (all females) as having "probable" rheumatoid arthritis according to the criteria of the American Rheumatism Association. Owing to withdrawals and other causes only 102 patients participated in the detailed analysis. Chloroquine diphosphate was given in doses of 250 to 500 mg. daily, using the double-blind technique. Clinical, radiological, and other assessments were made at entry and after treatment for one to 2 years; included were strength of grip in mm. Hg, haemoglobin concentration, erythrocyte sedimentation rate (Westergren), and sheep-cell agglutination test (S.C.A.T.).

Thirteen of the treated cases and 10 controls had symptoms ascribable to the drug, but on the whole side-effects were trivial. Two patients complained of visual disturbances, but as routine slit-lamp examination was not performed no information was available on the occurrence of corneal deposits as reported by other workers. A more serious complication (retinopathy and macular degeneration) has also been reported by others, but the authors consider that toxic effects are unlikely if the daily dose of chloroquine diphosphate does not exceed 250 mg. (150 mg. of base). There was a significant correlation between decrease in S.C.A.T. titre and clinical improvement, and a tendency for S.C.A.T. titre to fall after treatment, particularly in patients who had had the disease for only a short time. On the other hand it was

disappointing to find radiologically that the progress of joint damage seemed to be uninfluenced by the treatment. It is suggested that if a fall in S.C.A.T. titre is regarded as a favourable sign the known tendency for a rise in titre to follow steroid therapy could be counteracted by giving chloroquine in addition.

It is concluded that, apart from its ease of administration, chloroquine may be of some value as an adjunct in the conservative treatment of rheumatoid arthritis.

D. Preiskel

431. Studies on the Latex Fixation Test. (Studien über den Latex-Fixations-test)

H. SEIFERT. *Zeitschrift für Rheumaforschung* [Z. Rheumaforsch.] 20, 26-32, Feb., 1960. 4 refs.

Discrepancies between the results of the Rose-Waaler test and those of the latex fixation test have occasionally been noted by the author. This casts some doubt on the present concept that both of these tests depend on the presence of the rheumatoid factor in the serum. In a comparative investigation it was found that the results of the latex fixation test were in close agreement with the L-agglutination reaction against streptococci and those of the Rose-Waaler test with the γ -globulin reaction. In absorption experiments in which the heterohaemagglutinins and the rheumatoid factor were removed from a rheumatoid serum the Rose-Waaler and γ -globulin reactions became negative, whereas the latex fixation and L-agglutination reactions remained unchanged. It is concluded that the Rose-Waaler and γ -globulin reactions demonstrate the presence of the rheumatoid factor and the latex fixation test depends on a factor which agglutinates streptococci.

G. W. Csonka

GOUTY ARTHRITIS

432. Anturan in the Treatment of Gout

C. LUCEY. *Irish Journal of Medical Science* [Irish J. med. Sci.] 6, 113-121, March, 1961. 3 figs., 20 refs.

The treatment of 5 cases of primary gout with "anturan" (sulphinpyrazone) is reported from the Royal Victoria Hospital, Belfast. There were 4 men and one woman aged between 33 and 72 years. The initial dose was 50 mg. (half a tablet) 6-hourly given with meals, increased where possible to 100 mg. 6-hourly after 4 or 5 days, the object being to lower the serum uric acid level to normal and to keep it there. To avoid renal lithiasis the urine was kept alkaline by the administration of sodium bicarbonate, 20 gr. (1.3 g.) 6-hourly. Except for a reduction in caloric intake for the obese patients no specific dietary regimen was followed. Acute attacks in the early weeks were treated with colchicine. One patient given hydrochlorothiazide for oedema of the ankles during treatment with anturan showed a startling rise in serum uric acid level.

The mean reduction in serum uric acid level was 43%. All 5 patients felt improvement within a few weeks of starting treatment, including one patient with impaired renal function. Acute attacks of gout developed in 4 cases during the first few weeks of treatment, but, as the

author points out, this is liable to occur with any uricosuric agent. On the other hand the occurrence of oedema of the ankles in 2 cases was attributed to the anturan or the high sodium intake.

The author suggests that anturan is the most effective uricosuric agent at present available, and recommends its use for the routine treatment of gout.

G. S. Crockett

433. The Use of Sulfinpyrazone in the Treatment of Gout

R. H. PERSELLIN and F. R. SCHMID. *Journal of the American Medical Association* [J. Amer. med. Ass.] 175, 971-975, March 18, 1961. 11 refs.

Sulphinpyrazone ("anturan"), a uricosuric analogue of phenylbutazone, was administered over an average period of 14 months to 17 patients with gout, 2 of whom were in the chronic tophaceous stage of the disease, at the Medical Clinics of the Northwestern University Medical School, Chicago. The dosage was usually 400 mg. a day divided into 4 equal doses; colchicine was also given prophylactically in the initial months of treatment, but salicylates were prohibited.

Control serum uric acid values before treatment started averaged 8.7 mg. per 100 ml.; during therapy an average decrease of 37% to a mean value of 5.4 mg. per 100 ml. was obtained, the decrease ranging from 16% to 61%. (A spectrophotometric uricase method was used for the serum analyses.) The frequency of acute attacks of arthritis fell after 5 months' treatment, and in the final 5 months no attacks at all occurred. The toxicity of the drug is stated to be low; 2 patients developed a maculopapular rash, one a mild leucopenia, and 4 had dyspepsia which was relieved by taking the sulphinpyrazone with meals.

K. C. Robinson

434. Trimethylcolchicinic Acid in the Treatment of Acute Gout

S. L. WALLACE. *Annals of Internal Medicine* [Ann. intern. Med.] 54, 274-279, Feb., 1961. 1 fig., 22 refs.

This paper from the State University of New York College of Medicine, the Jewish Hospital, and Kings County Hospital, Brooklyn, New York, describes the results of treatment with trimethylcolchicinic acid (TMCA) in 34 cases of acute gout. Treatment consisted in the oral administration of 5 to 16 mg. of TMCA, usually in a single dose and within 4 hours to 3 weeks of the onset of the attack.

Response was complete or nearly complete in 26 cases (76%), partial in 4 (12%), and absent in 4 (12%). Four patients showing no response and 3 showing partial response were later treated with colchicine and 4 proved to be resistant. There was a tendency for a poor response to occur in those cases in which treatment had been delayed. Prophylactic therapy with TMCA in doses of 1 to 3 mg. daily was carried out in 7 cases. Although none of these patients developed an acute attack, it was considered that the period of observation (maximum 4 months) was too limited for an appraisal of the effectiveness of the drug as a prophylactic. Toxic effects were uncommon, with occasional mild nausea

(1 case) and mild diarrhoea (2 cases), and it is considered that TMCA compares favourably with colchicine for the treatment of acute gout.

Hewett A. Ellis

LUPUS ERYTHEMATOSUS

435. Intradermal Hypersensitivity in Systemic Lupus Erythematosus

J. C. BENNETT and H. L. HOLLEY. *Arthritis and Rheumatism [Arthr. and Rheum.]* 4, 64-73, Feb., 1961. 2 figs., 15 refs.

The authors, at the Medical College of Alabama, Birmingham, have studied the reaction of patients with systemic lupus erythematosus to intradermal injections of normal leucocytes. A positive reaction, maximal at 24 hours, occurred in 15 out of 17 cases of systemic lupus erythematosus, but in only 2 out of 40 cases of rheumatoid arthritis and in 1 case of rheumatic fever out of 26 cases of other diseases tested as a control. Histological studies of the injection sites were made in a number [unstated] of cases of systemic lupus erythematosus and control cases. In the former an inflammatory exudate of polymorphs and mononuclear cells tending to localize around blood vessels, degenerative nuclear changes, and some fibrinous transudate were seen, whereas biopsies from the control subjects showed only mild oedema with little inflammatory reaction.

M. Wilkinson

436. Renal Manifestations of Systemic Lupus Erythematosus; a Clinical and Pathological Study of 90 Cases

L. J. SOFFER, A. L. SOUTHERN, H. E. WEINER, and R. L. WOLF. *Annals of Internal Medicine [Ann. intern. Med.]* 54, 215-228, Feb., 1961. 15 refs.

This paper from the Mount Sinai Hospital, New York, describes the renal manifestations which occurred in 56 of 90 patients suffering from systemic lupus erythematosus (S.L.E.). All the patients had characteristic clinical and laboratory evidence of S.L.E., including a positive reaction to the L.E. cell test, and all those with renal involvement had persistent proteinuria, while 88% had haematuria, 63% pyuria, and 70% casts in the urinary sediment. Renal involvement was more frequent and severe in the younger patients, 35 instances occurring in those less than 30 years, of whom 16 died and 12 others had azotaemia. Of 21 patients over 30 years, 8 died, 9 had minor renal damage, and 4 had azotaemia. The longer the disease continued without renal involvement, the less likely was this to occur. Clinical features in the patients with renal involvement included the nephrotic syndrome (37%), hypertension (44%), oedema (35%), and abnormal fundi (30%). Pathological examination of the kidney in 19 cases showed that the degree of histological damage correlated with the severity of the clinical manifestations and the prognosis, but not with the blood urea level or 2-hour phenolsulphonphthalein excretion values.

Treatment with various steroids (for example, cortisone, initial dose 200 to 300 mg., maintenance dose 50 to 100 mg. daily; prednisone, initial dose 40 to 60 mg., maintenance dose 10 to 25 mg. daily) in doses sufficient

to control other symptoms of the disease failed to control the renal manifestations. Thus 26 of the 56 patients with renal involvement died, whereas none of the 26 patients without renal involvement who were followed up did so.

The study illustrates the serious prognosis in patients with renal involvement in S.L.E., even when treated with steroids. The authors suggest that more intensive and prolonged therapy might have favourably influenced the prognosis.

Hewett A. Ellis

437. Lupus Erythematosus: a Five-year Follow-up of 77 Cases

R. H. MARTEN and E. K. BLACKBURN. *Archives of Dermatology [Arch. Derm.]* 83, 430-436, March, 1961. 3 refs.

In a previous paper (*A.M.A. Arch. Derm.*, 1956, 73, 1; *Abstr. Wld Med.*, 1956, 20, 62) the authors reported haematological abnormalities in just over half of 66 cases of chronic discoid lupus erythematosus, in 5 out of 6 cases of generalized discoid lupus erythematosus, and in all 5 systemic cases seen in the Sheffield area between 1948 and 1952. The present paper deals with the clinical and haematological states of the same patients after a further 5 years of observation. Of the original 77 patients, 10 have died (but in only one case was death attributable to the lupus erythematosus), a further 9 could not be traced, and one patient had moved from the area, leaving the 57 patients who are the subject of the present survey.

Of 51 chronic discoid cases (38 female, 13 male), in 17 the disease was clinically inactive, 17 showed active and scarred lesions, and 17 active lesions only. Three of the 4 cases of generalized discoid disease and the 2 cases of subacute disseminated lupus erythematosus still showed active and scarred lesions. Haematological abnormalities were demonstrated in 30 cases of chronic discoid, 2 of generalized discoid, and 2 of subacute disseminated disease. These consisted in microcytic hypochromic anaemia (3 cases), leucopenia (4 cases), lymphopenia (4 cases), leucocytosis (one case), thrombocytopenia (6 cases), raised erythrocyte sedimentation rate (25 cases), and cold agglutinins (2 cases). In addition L.E. cells were found in the peripheral blood in 4 cases of chronic discoid, 2 of generalized discoid, and both cases of subacute disseminated lupus erythematosus. In all, 30 cases of chronic, 2 of generalized, and 2 of disseminated disease had some haematological abnormality.

In discussing their findings the authors comment on the increased number of chronic discoid cases which have become inactive, and they note again that there were no obvious clinical differences between the cases with abnormal and those with normal haematological findings. No cases of chronic discoid disease developed systemic lupus erythematosus, and only one case became generalized. In the period under review there was no evidence to suggest that cases of chronic discoid lupus erythematosus with haematological abnormalities are more likely to develop systemic manifestations.

Benjamin Schwartz

Neurology and Neurosurgery

438. Multiple Sclerosis: Assessment of Treatment with a Modified Low-fat Diet

R. L. SWANK and R. B. BOURDILLON. *Journal of Nervous and Mental Disease* [J. nerv. ment. Dis.] 131, 468-488, Dec., 1960 [received March, 1961]. 9 figs., 24 refs.

The senior author of this detailed report from the University of Oregon Medical School, Portland, has for several years been studying the effect of diets low in fats and containing 50% of vegetable or fish oils upon the progress of the disease in patients with disseminated sclerosis. The authors carefully analyse the difficulties in assessing the progress of the disease while under therapy and stress the need for obtaining "control" cases. This need, they conclude, can only be fulfilled at the present time by using the statistics of other authors. The statistical methods employed to assess and compare relapse rates and their significance in each case according to the state and duration of the disease are detailed.

The authors conclude that the low-fat diets recommended by them have benefited their patients. Thus they find the relapse rate reduced to very low figures after the patients had been on the diet for about 4 years. Also, those who began taking the diet within the first 5 years of their illness were improved, while those who began after this period were not. Moreover, a higher percentage of their patients were working and walking 10 years after the onset of their illness than in other authors' series.

[For a thorough understanding of the pitfalls of this type of therapeutic approach, and for a critical appreciation of the authors' findings and their significance, the reader is recommended to study the original paper, which is well documented.]

J. B. Cavanagh

439. Clinical Varieties of Writer's Cramp. (О клинических разновидностях писчего спазма)

K. F. KANAREJIN and I. S. KURILENKO. *Журнал Невропатологии и Психиатрии* [Ž. Nevropat. Psihiat.] 61, 62-66, No. 1, 1961. 9 refs.

The authors draw attention to variations in the symptoms of "writer's cramp" in different cases. While in the functional type the movements of writing only are involved, there are some cases in which the dystonia and spasm affect all complicated acts performed with the hand and wrist, such as shaving and fastening buttons. The latter form may be a manifestation of the early stages of a progressive organic disease of the central nervous system, such as epidemic encephalitis, hepatolenticular degeneration, or torsional dystonia, or of concealed trauma of the brain. Care should also be taken to distinguish between pure "classic" writer's cramp and a condition in which this is only part of a more generalized symptom complex in which agrammatism, paraphasia, lack of mental concentration or memory, or diminished space-perception are present. Case his-

tories are given in which clinical and electroencephalographic evidence was present of cerebral and striopallidal lesions. In yet-other cases the inability to write may be only part of a generalized neurosis.

L. Firman-Edwards

440. Painful Radiculopathy Treated with Epidural Injections of Procaine and Hydrocortisone Acetate: Results in 113 Patients

H. W. GOEBERT JR., S. J. JALLO, W. J. GARDNER, and C. E. WASMUTH. *Anesthesia and Analgesia; Current Researches* [Anesth. Analg. curr. Res.] 40, 130-134, Jan.-Feb., 1961. 1 fig., 11 refs.

Over the past 5 years the authors have used epidural injections for the treatment of sciatic and brachial radiculitis in patients seen at the Cleveland Clinic, Ohio. Of the 113 patients so treated, 3 received cervical, 9 thoracic, 15 lumbar, and the remainder caudal epidural injections. The injections were usually given on 3 consecutive or 3 alternate days, the solution generally employed being 30 ml. of 1% procaine combined with 125 mg. of hydrocortisone acetate, except for the cervical region, for which 10 to 15 mg. of procaine only was administered. Patients who had limitation of straight-leg raising were asked to exercise each leg alternately while the analgesic effect of procaine was present and to estimate the amount of relief obtained. A "good" result (60% relief for 3 months or longer) was obtained in 72% of patients, a "fair" result (40% relief for 3 months) in 11%, while the remainder were classed as "poor" results.

The findings are discussed in relation to the aetiology of radiculopathy and some theories are put forward to explain the mechanism of action of hydrocortisone. The authors suggest that the epidural injection of this steroid enables it to exert its anti-inflammatory action where it is most needed.

Mark Swerdlow

DIAGNOSTIC METHODS

441. The Electroencephalographic Diagnosis of Manifest and Latent "Delirium" with Particular Reference to that Complicating Hepatic Cirrhosis

J. LAIDLAW and A. E. READ. *Journal of Neurology, Neurosurgery and Psychiatry* [J. Neurol. Neurosurg. Psychiat.] 24, 58-70, Feb., 1960. 5 figs., 18 refs.

It is recognized that the electroencephalogram (EEG) follows a fairly well-defined series of changes as a patient passes into coma and that this is particularly apt to occur in hepatic cirrhosis. These patients are liable to episodes of confusion or alteration of consciousness; this state the authors term "delirium" and the tendency to develop this condition they call "encephalopathy". Writing from the Postgraduate Medical School of London, they

describe a method, based on electronic analysis, of assessing the rhythmic background activity of the EEG and emphasize the importance of following this through a series of records. They show how the EEG may be modified by changes in the level of protein intake and that provocative doses of morphine (8 mg.) could be safely given to such patients in order to bring out the EEG changes.

They suggest that this method can be used as a diagnostic tool, not only to help in determining the cause of a delirium, but also to pick out the patients with mild encephalopathy. These patients may show no clinical or EEG abnormalities, but in them the EEG changes of delirium may be provoked by the measures described, often without producing any clinical change and at no risk to the patient.

[This is not an easy paper to follow; in view of so many variables, not only in the EEGs from different grades of patient but also the variations in diet and provocative agents, it needs very careful reading to appreciate all the authors' points.] N. S. Alcock

442. Asymmetries of Beta Activity in Epilepsy, Brain Tumour, and Cerebrovascular Disease

R. L. GREEN and W. P. WILSON. *Electroencephalography and Clinical Neurophysiology* [Electroenceph. clin. Neurophysiol.] 13, 75-78, Feb., 1961. 12 refs.

The electroencephalograms of a group of patients suffering from epilepsy, vascular disease, or space-occupying lesions, were examined at the Veterans Administration Hospital and Duke University School of Medicine, Durham, N. Carolina, for voltage asymmetries of 50% or more in beta activity (14 to 30 c.p.s.). In 7 cases of subcortical epilepsy no asymmetry was noted, but in 16 out of 93 cases of cortical epilepsy an asymmetry was evident. In 15 of these the beta activity was of higher amplitude on the same side as the epileptiform discharges; in the remaining case it was of higher amplitude on the opposite side. In 26 patients with occlusive vascular lesions involving the anterior and posterior cerebral arteries the beta activity remained symmetrical, but among 39 with infarction in the territory of the middle cerebral artery asymmetry was noted in 9. In 7 of these the higher voltage occurred on the same side as the lesion. Among 55 patients with space-occupying lesions the beta activity was of higher voltage on the affected side in 21 and on the opposite side in 4. The authors believe that lesions such as glial scars and infiltrating tumours tend to potentiate beta rhythm, perhaps by increasing the activity of adjacent cell areas.

[This hypothesis is supported by the statement that lesions such as meningioma and subdural haematoma which compress the cortex are unaccompanied by beta asymmetry. Elsewhere the 2 cases of subdural haematoma included are shown as having an increased beta amplitude on the side of the lesion. The classic paper of Pampiglione (*Electroenceph. clin. Neurophysiol.*, 1952, 4, 79) is not quoted. Pampiglione emphasizes the frequency with which diminution of beta activity occurs in the neighbourhood of cerebral lesions and stresses the diagnostic value of this finding.] L. G. Kiloh

443. The Electroencephalogram in Cerebral Vascular Disease

R. M. PADDISON and G. S. FERRISS. *Electroencephalography and Clinical Neurophysiology* [Electroenceph. clin. Neurophysiol.] 13, 99-110, Feb., 1961. 8 figs., 13 refs.

This paper from Louisiana State University School of Medicine, New Orleans, reports an electroencephalographic investigation of 138 cases of cerebral arteriosclerosis. No cases of primary intracerebral haemorrhage were included. Localized infarcts were present in 67 patients. Amongst these the electroencephalogram (EEG) proved abnormal in 5 of 6 cases of internal carotid arterial occlusion, in 26 of 39 cases of infarct in the territory of the middle cerebral artery, in 2 cases of involvement of the posterior cerebral artery, and in 6 of 20 cases of lesions in the distribution of the vertebro-basilar system. The diagnosis of cerebral ischaemia was made when focal signs disappeared within a few days of their onset. In such cases the EEG was abnormal in 5 of 13 cases affecting the carotid system; carotid compression in those with normal EEGs was judged to produce abnormalities in 3 cases. In none of 7 cases of ischaemic changes affecting the vertebro-basilar system was the EEG abnormal, nor did carotid compression have any effect in the 3 cases in which it was tried. Of 50 cases of generalized cerebral arteriosclerosis, abnormalities were found in the EEG in 22.

The authors conclude that electroencephalography is a valuable diagnostic aid in cerebrovascular disease and that carotid compression is of value both in estimating the relative importance of each vessel to the total cerebral circulation and the extent to which further ischaemia can be sustained.

[The most valuable part of this paper is the review of the literature. As the authors admit, no patho-anatomical or statistical correlates can be drawn from their data. The time relation of the EEG recordings to the clinical events is not stated, though it is mentioned that the elapsed time varied from a few hours to years.]

L. G. Kiloh

BRAIN AND MENINGES

444. Possible Mechanism of Action of Hypertonic Urea in Reducing Intracranial Pressure

T. W. LANGFITT. *Neurology* [Neurology (Minneap.)] 11, 196-209, March, 1961. 4 figs., bibliography.

The author, working at Johns Hopkins University, Baltimore, set out to assess the mechanism of, and variability in individual response to, urea administered intravenously to reduce the intracranial pressure in the performance of brain surgery. He first reviews various hypertonic agents which are used to reduce intracranial pressure, outlining the apparent advantages and drawbacks of sodium chloride, glucose, sucrose, sodium arabinates, and urea, and then describes his experimental observations on 10 patients with intracranial disease, 8 of whom were in stupor or coma, but none of whom had marked increase in intracranial pressure. In addition to measurements of the lumbar cerebrospinal fluid (C.S.F.) pressure, numerous chemical analyses of the serum,

C.S.F., and urine were carried out, both before and at intervals after the intravenous infusion of a solution of 25 to 30% lyophilized urea in 5% dextrose and water or in 10% invert sugar, the dose being 0.5 to 1.5 g. per kg. body weight given within 30 minutes.

It was found that a rapid and marked fall in C.S.F. pressure occurred in all subjects, but half the patients showed a subsequent rebound or secondary elevation of C.S.F. pressure above the control level. The degree of fall in pressure appeared to correlate less with the dose of urea given than with the initial C.S.F. pressure. One patient exhibited transient haemoglobinuria, but otherwise no untoward reactions were observed.

J. B. Stanton

445. Clinical Features and Pathological Anatomy of Lesions in the Reticular Formation of the Medulla Oblongata. (К клинике поражения и патологической анатомии ретикулярной формации каудального отдела продолговатого мозга)

V. I. ŠARAPOV. *Журнал Невропатологии и Психиатрии* [Z. Neuropat. Psychiat.] 61, 11-18, No. 1, 1961. 4 figs., 26 refs.

The author describes 2 cases of bulbar paralysis, together with the histological findings in the brain after death. One was in a woman of 31, the other in a young man of 16; both patients presented with dysphagia, oedema of the face, arms, and chest, progressive weakness, and loss of power to walk, sit, or stand—at first intermittent and later complete. The woman had pyrexia and pains in the joints at the onset of her illness, and patches of psoriasis developed on her arms and chest; the young man had neither of these signs, but the mucosa of his mouth was covered with small ulcers. In neither case was there sphincter involvement, sensation was unimpaired, and consciousness was normal. Death ensued 5 and 6 months respectively after the onset.

The histological findings were identical in the 2 cases; no changes were found in sections from any part of the brain or spinal cord except the medulla oblongata. The lesions were confined to the nuclei of the vagus nerve and the fasciculus solitarius and to the fibres of the reticular formation. There was yellow pigment in the protoplasm of the cells of the vagal nuclei, with deformation of the nucleus and displacement of the nucleoli; neuronophagia was marked. The cells of the fasciculus solitarius were oedematous, the protoplasm being filled with Nissl substance. In places there was lymphocytic infiltration. In some parts of the nucleus of the hypoglossal nerve the cells were oedematous.

Apart from the bulbar symptoms there was almost complete loss of muscular tone, due to disturbance of the suppression of impulses from the formatio reticularis to the lower motor neurones and to the cerebral cortex. At the same time the sympathetic links with the vagus nerve were interrupted. Magoun and Rhines (*J. Neurophysiol.*, 1946, 9, 165) have shown that the formatio reticularis sends inhibiting impulses to the spinal motor centres, depressing them and reducing muscular tone. The oedema of the face, arms, and chest, as also the psoriasis, were presumably manifestations of trophic disturbance.

L. Firman-Edwards

446. A Case of Disturbance of Musical Expression following Severe Head Injury. (Ein Fall mit gestörter musischer Expression nach schwerem Schädeltrauma) K. KRYSPIN-EXNER and K. WEINGARTEN. *Wiener Zeitschrift für Nervenheilkunde und deren Grenzgebiete* [Wien. Z. Nervenheilk.] 18, 253-262, 1961. 2 figs., 18 refs.

A case of head injury with motor aphasia and right hemiplegia is described in which, after recovery from the aphasia, the patient could no longer speak in dialect, but only in "school" German, sounding somewhat like a foreigner. At the same time he had a disturbance of singing and difficulty in the finding of melodies, although his understanding of music remained intact and he could recognize tunes easily. The difficulties of classification of this type of case, of which others have been reported in the past, are discussed. The condition could either be conceived as a case of polyglot aphasia or as dysprosody (Monrad-Krohn). Further, the relationship between this type of speech disorder and expressive amusia is not clear, nor is the question of localization. Many authors consider these disturbances to be due to a generalized dysfunction. According to Kleist, however, the lesion is in the pre-frontal lobes and must be bilateral. In the present case there was evidence of bilateral frontal lesions.

J. Hoenig

447. Urea in the Management of Head Injuries E. S. WATKINS, J. D. STUBBS, and W. LEWIN. *Lancet* [Lancet] 1, 358-363, Feb. 18, 1961. 4 figs., 12 refs.

Writing from the Radcliffe Infirmary, Oxford, the authors stress the important part played by raised intracranial pressure in the prognosis of cases of severe head injury, whether this pressure is due to intracerebral haematoma or non-specific cerebral oedema, and briefly review previous methods adopted to reduce intracranial pressure, as for example the use of rectal infusions of magnesium sulphate. They also note the part played by tracheostomy and hypothermia in the improving prognosis of these cases and endorse views previously expressed that urea is superior to other agents in reducing intracranial pressure.

They then describe a series of 30 patients (including 3 treated at the Army Neurosurgical Unit, Wheatley, Oxfordshire) who were given intravenous urea out of a total of 1,046 cases of acute head injury seen between March 1, 1959, and May 31, 1960. All 30 patients were comatose at the beginning of treatment and all were considered to have raised intracranial pressure, this being confirmed at operation. They describe the benefit afforded by intravenous urea in operating on cases of acute subdural haematoma, generalized cerebral oedema, postoperative cerebral oedema, and the temporal lobe syndrome. They suggest that in patients with severe brain injuries urea will have its greatest effect when cerebral oedema, rather than contusion or laceration, predominates. They describe in detail their technique of injection and discuss briefly the mechanism of action of this hypertonic solution. They stress the danger of inadvertent injection into soft tissue, which may lead to sloughing and necrosis; the danger of masking an intracranial haematoma, when a patient with such a lesion

responds to the intravenous urea and the obvious clinical improvement results in the true diagnosis being missed; and lastly the danger of circulatory collapse in patients suffering from cardiovascular disease or diabetes. Finally they draw attention to the metabolic disturbance caused by this powerful hypertonic solution and to the danger of this in patients with impaired renal function or with incipient hepatic failure.

J. B. Foster

448. The Little Stroke. A Report on 89 Cases

B. H. McCONNELL. *Journal of the American Geriatrics Society [J. Amer. Geriat. Soc.]* 9, 110-118, Feb., 1961. 43 refs.

In view of the suggestion that so-called "little strokes" are due to damaged cerebral capillaries, the author of this paper from Florida Southern College, Lakeland, Florida, treated a group of 89 patients with a past history of one to 4 incidents with a water-soluble citrus bioflavonoid compound containing 100 mg. of bioflavonoids and 100 mg. of ascorbic acid per capsule ("CVP"). A control group of 62 patients received other treatment, but not CVP. Cases of suspected or confirmed cerebral arterial occlusion were excluded. The capillary fragility, which was estimated in all patients, was unchanged after 6 months in the control group, but was much reduced in the majority of patients given CVP. During a follow-up period of one to 5 years there were 3 cases of little stroke but no deaths among the 89 patients given CVP, while in the control group there were 18 cases of severe stroke including 5 deaths and 12 cases of little stroke. The author concludes that CVP had a beneficial effect in reducing the number of recurrent little strokes, and believes that the results of the study lend support to the view that embolism and occlusion are relatively rare phenomena in little stroke and that capillary bleeding is the true and most frequent cause of this condition.

[The value of this study is lessened by the author's failure to define "little stroke" and its clinical differentiation from cerebral arterial occlusion, by the omission of any description of the basis of selection of patients and controls, and by lack of precise data on the dosage of CVP and on the other therapeutic measures employed.]

Bernard Isaacs

449. Fibrinogen Changes in Relation to Cerebrovascular Accidents

F. A. ELLIOTT and M. BUCKELL. *Neurology [Neurology (Minneapolis)]* 11, 120-124, Feb., 1961. 1 fig., 25 refs.

The serum fibrinogen level was estimated serially in 24 patients admitted to the Pennsylvania Hospital, Philadelphia, suffering from recent cerebrovascular accidents. Single control observations were made on 41 patients of similar age range suffering from diabetes or hypertension who had not sustained strokes. The range of fibrinogen content in the control group was 130 to 550 mg. per 100 ml., with a mean of 330 mg. per 100 ml. In 22 of the 24 cases of stroke the serum fibrinogen level began to rise 2 to 4 days after the acute episode and reached a peak between the 4th and 14th days, thereafter slowly falling again. The height to which the level rose was related to the outcome. Thus of 12 patients whose

serum fibrinogen content reached 700 mg. per 100 ml. 6 died in hospital and only one became fit to look after himself, while of the remaining 12, whose fibrinogen level did not reach 700 mg. per 100 ml., only one died and 8 became independent. The authors refer to the difficulty of being sure that the rise in fibrinogen level was not due to pulmonary or urinary infection, but give grounds for their belief that in their cases the rise was largely a function of cerebral damage. They consider that a rise in the serum fibrinogen level above 700 mg. per 100 ml. is of serious prognostic significance in cases of stroke.

Bernard Isaacs

450. Evaluation of Controlled Digital Artery Compression in Cerebral Vascular Insufficiency: the Ischemic Response

J. McBEATH, R. WINSTON, and W. J. FRIEDLANDER. *Neurology [Neurology (Minneapolis)]* 11, 143-150, Feb., 1961. 4 figs., 25 refs.

The effects of digital compression of the carotid arteries for 30 seconds were studied in a group of 446 patients at the Veterans Administration Hospital, Boston. Of these patients, 166 had clinical evidence of cerebral vascular insufficiency (C.V.I.) and some had angiographic evidence as well, while the remaining 280 had no evidence of C.V.I. An ischaemic response to carotid compression was defined as the appearance of obvious slow activity in at least one lead of the electroencephalogram during compression.

Ischaemic responses occurred more frequently when C.V.I. was present than when it was absent. This difference was statistically significant in patients under the age of 60, but was not significant in those over 60. In the latter group ischaemic responses were significantly more frequent among patients with insufficiency of the basilar tree than among those with no evidence of C.V.I. In patients with partial occlusion of the carotid artery ischaemic responses were obtained by compressing either the affected or (more often) the opposite, unaffected, vessel, whereas in those with total occlusion of one carotid artery ischaemic responses were elicited only by compression of the unaffected vessel. The procedure was not without danger, since 2 patients developed hemiparesis a few hours after the compression. One of these patients recovered after a week but the other remained paralysed.

The authors consider that an ischaemic response to carotid compression in the absence of clinical evidence of C.V.I. may indicate a defect of the collateral circulation, for which the term "subclinical C.V.I." might be used. They are conducting a follow-up study to determine the prognostic value of this sign.

Bernard Isaacs

451. Kinking of the Internal Carotid Artery in Relation to Cerebrovascular Disease

H. METZ, R. M. MURRAY-LESLIE, R. G. BANNISTER, J. W. D. BULL, and J. MARSHALL. *Lancet [Lancet]* 1, 424-426, Feb. 25, 1961. 1 fig., 8 refs.

A series of 1,000 consecutive angiograms were examined by the authors at the National Hospital, Queen Square, London, to determine the incidence, aetiology,

and connexion with cerebrovascular accidents of kinks of the internal carotid artery in the neck. A kink is defined as a complete loop or an angle between the two segments of 90° or less. Kinks were present in 161 (16%) of the angiograms and these cases were subdivided into 3 groups according to the severity of the deformity. The incidence did not increase with advancing age or rising blood pressure and therefore a developmental anomaly is postulated as the most likely aetiological factor. Of the 60 patients in Group III (loop or angle >30°), 14 had suffered from vascular accidents in the past and 4 of them from recurrent episodes. Comparison of this group with a group of 60 patients selected at random from among those without kinks showed that cerebrovascular accidents were more frequent in the presence of a kink, but the difference was not statistically significant. Recurrent episodes did not occur in the control group, but the P value (0.059) for this difference was outside the conventional 5% level of significance; nevertheless the odds that the findings were due to chance are 17 to 1 against.

A total of 24 patients in Group III, 4 of whom had had a previous cerebrovascular accident, were re-examined. In 4, one of whom had previously had a cerebrovascular accident, rotation of the neck produced symptoms. The side of the symptoms had no relation to the kink or direction of neck rotation. The degree of kinking appeared to vary with the position of the neck. Although the evidence is not indisputable, it is suggested that a kinked carotid artery may produce recurrent cerebrovascular episodes. The relevant factor for the production of symptoms may be an atherosclerotic plaque at the site of the kink. Surgical excision should be considered in patients with recurrent cerebrovascular episodes who have a kink in the carotid artery and in whom no other adequate abnormality can be found.

H. S. Schutta

452. Cerebellar Manifestations and Cerebellar Lesions in Epilepsy. (Manifestations cérébelleuses et lésions cérébelleuses chez les épileptiques)

J. ROGER, H. PAYAN, M. TOGA and R. SOULAYROL. *Revue neurologique* [Rev. neurol.] 103, 410-428, Nov., 1960 [received March, 1961]. 6 figs., 30 refs.

In this paper from the Faculty of Medicine, Marseilles, the authors summarize 6 cases reported in the literature and describe 6 personal cases of a progressive cerebellar syndrome developing usually in patients with chronic epilepsy of at least 15 years' duration who also manifest other neurological and mental changes. In one of their own cases, in a woman aged 24 years, however, the syndrome appeared only 2 years after the onset of epilepsy. Pathological findings are also described in 13 epileptics who exhibited cerebellar atrophy in addition to cerebral changes at necropsy. These included degenerative changes in the Purkinje cells, with diminution of the shadow cells, and more rarely diffuse or focal pallor of the granular layer, with gliosis of the molecular layer. The authors conclude that ischaemic changes resulting from repeated vascular compression during the fits initiates abiotrophic changes in those with a hereditary predisposition.

I. Ansell

CRANIAL NERVES

453. The Accessory Facial Nucleus and Its Interconnections with the Main Nucleus in Man. (О добавочном ядре лицевого нерва и о перекресте корешковых волокон его главного ядра у человека)

S. M. BLINKOV. *Журнал Невропатологии и Психиатрии* [Z. Nevropat. Psihiat.] 61, 265-270, No. 2, 1961. 2 figs., 24 refs.

The accessory facial nucleus was first described in 1893. Situated as it is between the main nuclei of the 6th nerve above and the 7th nerve below, there was some doubt as to which it belonged. Thus Vyubov and also van Valkenberg regarded it as part of the 7th (facial) nerve, whereas van Gehuchten and others related it to the 6th (abducens). Even in recent atlases these divergent views are still expressed by different authors.

The opportunity of examining post mortem the brains of 2 patients with auditory nerve tumours has presented the present author with strong evidence that this small nucleus is in fact part of the facial nerve, this being based on examination of a large series of sections stained by thionin, haematoxylin, and haematoxylin plus picrofuchsin. In both cases the tumour had been removed from the left side, with consequent injury to the root of the left facial nerve. Retrograde degeneration had taken place in the chief nucleus, some 50% of the motor cells of the left side and 1% of those of the right side being involved. All the cells of the accessory nucleus in one case and half of them in the other also showed retrograde degeneration. There was, however, no such change in the nucleus of the abducens nerve.

Vyubov had also shown that in injury to the facial nerve from infection in the Fallopian canal both the main nucleus and the accessory were involved. In the author's opinion this finding is more convincing than the observations of Kaplan and Finkelnburg that no cells could be seen in the accessory nucleus of a patient with atrophy of the nucleus of the abducens nerve of the same side. He considers this might easily have been due to error, since the accessory nucleus extends only a short distance in the oro-caudal direction and the number of its cells is very variable, ranging from 20 to 330. No one has so far reported the finding of degeneration of the cells of this nucleus in association with degeneration of the 6th nerve in man, although van Gehuchten demonstrated it in rabbits. But it cannot be assumed that the accessory nucleus in man is homologous with a similar nucleus in other vertebrates. However, Terni (*Folia neuro-biol. (Lpz.)*, 12, 277 [no year given]) concluded that the nucleus innervated the nictitating membrane and the retractor bulbi muscle in reptiles. Szentagothai, in a series of experiments on cats, showed that it innervates the posterior belly of the digastric muscle. It may therefore be concluded that in man, and also in at least some animals, the accessory nucleus is part of the 7th cranial nerve; and from the very small proportion of heterolateral cells found to be degenerated in his 2 cases (1% in one case and 0.8% in the other) the author concludes that very little crossing of fibres takes place.

L. Firman-Edwards

Psychiatry

454. **Diurnal Variations in Mood and Drive in Healthy Persons.** (Die tagesrhythmischen Schwankungen der Stimmung und des Antriebes beim gesunden Menschen) H. HAMPP. *Archiv für Psychiatrie und Nervenkrankheiten* [Arch. Psychiat. Nervenkr.] 201, 355-377, 1961. 3 figs., 49 refs.

The diurnal variations in mood and drive were assessed at the University Neurological Clinic, Munich, in 400 healthy persons, namely, 50 doctors, 100 students, 100 male and female non-manual workers, 100 male and female manual workers, and 50 farmers, since such variations are considered to provide an important diagnostic criterion in the depressive psychoses, but have never been systematically assessed in a normal population. In the present investigation an attempt was also made to relate these phenomena to social groups and the different modes of life in such groups.

It was found that 52% of all the subjects had noted diurnal rhythmicity and 39% had not, while 9% related them to events in their environment and thus considered them entirely psychogenic. In one-third of all cases the peak of drive was experienced in the evening, and in one-fifth in the morning. The subjects unaware of any rhythmicity showed the following social distribution: manual workers 49%, non-manual workers 36%, and professional workers 30%. The peak occurred in the evening in 46% of the professional group, in 26% of manual workers, and in 29% of non-manual employees, while a morning peak was noted by 14% of the professional group, 14% of the manual workers, and by 28% of non-manual employees. The amount of sleep required was somewhat greater in those with a marked evening peak, but in general there did not appear to be a definite relationship between the amount of sleep and type of rhythmicity. The relationship of these findings to the diurnal variations in patients with endogenous depression is discussed, the author pointing out that not only are the variations in psychotics much more marked, but they are also subjectively experienced in a different way by the patients.

J. Hoenig

455. **Deviant Sexual Behaviour and the Sex Criminal**

H. PASCOE. *Canadian Medical Association Journal* [Canad. med. Ass. J.] 84, 206-211, Jan. 28, 1961. 11 refs.

Some aspects of deviant sexual behaviour and a few typical case histories are discussed in this paper from the University of Alberta, Edmonton, Canada. Attention is drawn to the fact that as regards various "crimes" or antisocial behaviour individuals can be differentiated on the basis of whether they "care" or have "conscience" about right and wrong, but this does not always apply in sexually deviant behaviour, where the act is usually between two mutually consenting parties—for example, homosexuality. From his experience of those who are habituated to partaking in sexually deviant be-

haviour the author considers that in most of them the main aetiological factor is "castration anxiety" and feelings of inadequacy concerning their own masculinity. This leads them to seek sexual gratification by means other than those of heterosexual relationships with a mature female partner.

Discussing treatment, the author states that various methods have proved useful, but the two main factors which seem to influence the outcome of treatment are: (1) whether or not the subject is sincerely desirous of ridding himself of his abnormality, and (2) whether or not the subject has a "moral and social conscience", lack of which is prognostically poor.

[Since social and environmental factors significantly influence individual behaviour in relation to society, and since it is well known that many sex deviants show satisfactory heterosexual relationships, to explain sexual deviation mainly on the basis of castration anxiety does not appear justified from the data presented. It is legitimate therefore to suggest that any explanation of such behaviour without consideration of these factors is inadequate.]

N. Rathod

456. **Investigations into the Interrelation of Physical and Mental Retardation**

M. REISS, H. H. BERMAN, J. J. PEARSE, K. ALBERT-GASOREK, and J. C. HILLMAN. *Journal of Neuropsychiatry* [J. Neuropsychiat.] 2, 109-137, Feb., 1961. 12 figs., 27 refs.

This study from Willowbrook State School, Staten Island, New York, records the evidence of physical and mental immaturity in 102 retarded patients and attempts to correlate biochemical, endocrinological, physical, and psychiatric findings both before and after treatment. The results are also given of detailed longitudinal studies on 10 representative patients who were treated with chorionic gonadotrophin and triiodothyronine.

In general, while the patients did not form a homogeneous group, hypopituitarism was often a cause of their physical retardation. Chorionic gonadotrophin speeded up longitudinal growth and also caused maturation of the body. The behavioural changes that occurred during treatment are also described, as are the changes in psychological test results. [The original paper should be consulted for details.]

B. M. Davies

457. **Adrenal Steroid Excretion Patterns in Eighteen Healthy Subjects: Tentative Correlations with Personality Structure**

H. M. FOX, B. J. MURAWASKI, A. F. BARTHOLOMAY, and S. GIFFORD. *Psychosomatic Medicine* [Psychosom. Med.] 23, 33-40, Jan.-Feb., 1961. 10 refs.

This study of adrenal steroid excretion patterns in relation to personality was carried out at the Harvard School of Public Health and the Peter Bent Brigham

Hospital, Boston, on 18 healthy male students over a 5-week period, the urinary excretion of 17-hydroxycorticosteroids and 17-ketosteroids being determined daily on 24-hour specimens of urine. The data were treated statistically by the technique of analysis of variance. The subjects were also studied psychologically by means of tape-recorded interviews and subjected to the Rorschach test, and an attempt was made in each case to correlate the personality findings with the urinary steroid levels.

It was found that the 24-hour excretion rates of both steroids remained relatively constant during the period of observation and that each individual throughout maintained his same relative position in regard to the whole group. When the 17-hydroxycorticosteroid excretion values rather than the 17-ketosteroid levels were used as a basis for psychophysiological correlation it emerged that the former could be associated with certain features of personality, the findings indicating that the more an individual reacts emotionally, the higher the urinary output of 17-hydroxycorticosteroids and vice versa. It is suggested that the relative constancy of adrenal steroid excretion in each individual depends on genetic or constitutional factors and that these "may prove significant for the future adaptation of these individuals to stress and disease".

A. Balfour Sclaire

MENTAL DEFICIENCY

458. **The Puff Test: an Attempt to Assess the Intelligence of Young Children by Use of a Conditioned Reflex**
J. RENDLE-SHORT. *Archives of Disease in Childhood* [Arch. Dis. Childh.] 36, 50-57, Feb., 1961. 15 refs.

Using a standard puff of air, the apparatus for which is fully described, the author has tested the blink-reaction of 155 children of apparently normal intelligence aged from 5 months to 7 years and 74 mentally defective children with chronological and mental ages ranging from under 6 months to over 6 years. A score was obtained by recording the number of puffs required to establish a conditioned reflex, this being recognized by the child blinking on presentation of the puff-gun, although no puff was actually produced.

Of 12 normal children aged 6 months or less, 11 could not be conditioned after exposure to 20 puffs—the normal infantile response. Of 49 aged between 6½ and 12 months, 15 gave the infantile response, the others requiring up to 13 puffs; of 32 aged between 12½ and 18 months, all were conditioned by 11 or fewer puffs with the exception of one who required 19; and of 47 aged between 18 months and 4 years, 45 were conditioned by 2 to 6 puffs, 2 requiring more; lastly the normal adult response of conditioning after 2 puffs was shown by 13 out of 15 children over the age of 4 years. Scattergrams of the results for the mentally defective children showed little resemblance to those for the normal children in regard to chronological age, but some resemblance in respect of mental age. Over the series as a whole no simple relationship between ease of conditioning and age or intelligence could be established, but there was an

almost linear relationship between ease of conditioning and age in normal children up to about 5 years of age. The author suggests that the puff test is of value in estimating the intelligence of young children up to the age of 4, including those with spasticity or deafness, but not of course those who cannot see. It is quick to perform, usually taking only 2 or 3 minutes and never more than 7, and requires the minimum of cooperation on the part of the subject.

G. de M. Rudolf

459. **A Survey of a Group of Children with Mental and Physical Handicaps Treated in an Orthopaedic Hospital**
E. P. QUIBELL, E. STEPHEN, and E. WHATLEY. *Archives of Disease in Childhood* [Arch. Dis. Childh.] 36, 58-64, Feb., 1961. 9 refs.

The authors have attempted to evaluate the response to treatment of 40 educationally subnormal (and ? ineducable) children aged from 2 to 16 years who had been in Chailey Heritage Hospital, Sussex, for at least one year. Of these, 30 had cerebral palsy, 7 spina bifida, and the other 3 had poliomyelitis, toxoplasmosis, and phenylketonuria with poliomyelitis respectively. Assessments were made of daily living functions (speech, ambulation, washing and dressing, feeding, toilet management, and fine hand activities), emotional adjustment, educational attainments, and home conditions. The children were divided into four groups: (1) those now functionally independent for daily living, (2) those ambulant but not entirely independent, (3) those "requiring ward placement" but improving, and (4) those making no worth-while progress.

In Group 1 (11 children aged from 8 to 15 years) 7 improved in daily living functions and 4 who were unable to walk on admission became fully ambulant. In Group 2, of 10 children aged between 9 and 16 years, all showed improvement in daily living, 5 previously unable to walk became fully ambulant, and none is now unable to read. In Group 3 (13 patients from 2 to 14 years old of whom 11 were treated) 4 can now walk slowly, 6 can walk a few steps with crutches, 5 improved in speech, 4 in contacts, 4 began to use nursery apparatus, 4 have improved in washing and dressing, 3 can feed themselves, 3 have become clean and dry, and 2 have progressed in regard to fine hand movements. Of the 6 patients in Group 4, aged between 6 and 15 years, 3 were educationally subnormal and 3 were untestable and no conclusions could be drawn. The time required to achieve ambulation varied from 5 months to 6 years. In a special assessment of the emotional adjustment of 17 boys (13 ambulant and educationally subnormal and 4 severely handicapped and educationally subnormal) 3 were considered to be emotionally well adjusted, 12 mildly maladjusted, and 2 grossly maladjusted; 6 showed a tendency to outgoing aggressive behaviour and 4 to passive withdrawn behaviour. Their reading ages range from 11 to 5 years and arithmetic ages from 9 to under 5 years.

No relation between adverse social factors and failure to make progress was found. Many children with adverse factors such as broken homes, early separation from their family, and long periods in hospital improved and showed only minor degrees of maladjustment. This,

it is suggested, may be due to the warm relations which exist with the staff, stimulating daily programmes, and maintenance of links with the patients' families. The authors conclude that the minimum I.Q. (in this investigation 41) necessary to make useful progress in daily living function is much lower than has been previously assumed, and that imbeciles may make some response but idiots probably not.

[For a great number of years idiots have progressed in habits of cleanliness and obedience in hospitals for the mentally subnormal.]

G. de M. Rudolf

460. Studies on 5-Hydroxyindole Metabolism in Autistic and Other Mentally Retarded Children

R. J. SCHAIN and D. X. FREEDMAN. *Journal of Pediatrics* [J. *Pediat.*] 58, 315-320, March, 1961. 1 fig., 25 refs.

It is thought likely that the biogenic indole alkylamine 5-hydroxytryptamine (serotonin) plays some role in neuronal function in the brain, although the nature of this role has not been clarified. In this study, reported from Yale University School of Medicine, the blood levels of 5-hydroxytryptamine (5-HT) and urinary excretion of 5-hydroxyindoleacetic acid (5-HIAA) were determined in 23 patients aged from 6 to 18 years who had been diagnosed as cases of infantile autism on the grounds of severe preoccupation with self and unrelatedness to other people, a history of onset during the first 2 years of life, and the absence of a history of serious motor retardation. In addition 12 mildly retarded (I.Q. 60 to 80) and 5 severely retarded (I.Q. under 20) non-autistic children were similarly examined, multiple estimations being made in each case. Blood was withdrawn in the afternoon, frozen for up to 24 hours, 5-HT extracted with 20 volumes of acetone, and the extract dried *in vacuo* and kept at -18°C . until bioassay on the heart of the clam or the rat uterus in oestrus could be performed.

The mean normal blood 5-HT levels were 0.02 to 0.15 μg . per ml. Of the 23 autistic patients, 7 showed values above normal, rising to 0.54 μg . per ml. In both mildly and severely retarded non-autistic children the mean values were normal, although the severely retarded gave a higher mean value than did the mildly retarded. Loading with tryptophan in 4 of the autistic children produced no consistent change in 5-HT level, nor was the administration of phenobarbitone, "dilantin" (phenytoin sodium), or chlorpromazine associated with any change in 5-HT levels. The authors state that the 24-hour urinary excretion of 5-HIAA probably fell in most cases within the generally accepted values of 2 to 9 mg., although the values were distinctly higher in 12 autistic children than in 6 mildly retarded children; creatinine values were much lower in the autistic children, indicating greater dilution of the urine. The symptomatology in the 6 autistic children with the highest blood 5-HT levels did not differ from that in the other autistic patients with normal levels, except that, perhaps significantly, none of them suffered from the seizures which are usually a frequent occurrence in autistic children.

[A scattergram shows great variations in the successive values of 5-HT for each subject, ranging from 0.21 to

0.54 μg . per ml. As it is known that 5-HT decays rapidly in brain tissue the possibility exists that this may also be true for blood. The authors do not state the individual times of storage of blood before extraction.]

G. de M. Rudolf

ORGANIC DISORDERS

461. Meprobamate-Promazine Therapy for Aged Psychiatric Patients with Chronic Brain Syndrome Associated with Arteriosclerosis

V. L. KOZLOWSKI. *Journal of the American Geriatrics Society* [J. *Amer. Geriat. Soc.*] 9, 376-380, May, 1961.

Striking improvement in the mental condition of 21 (81%) of 26 patients who had chronic brain syndrome associated with cerebral arteriosclerosis with psychosis and behavioral problems was obtained with the use of combined meprobamate-promazine therapy. The remaining 5 patients showed some improvement, in that they became more quiet, calm and cooperative. The amount of the combined meprobamate-promazine medication required to produce improvement did not give rise to the severe side-effects frequently noted with the use of individual tranquilizers and sedatives. The combined medication facilitated the control and management of these patients, made them more amenable to psychotherapeutic and rehabilitation programs, and was an excellent adjunct to psychotherapy.—[Conclusions.]

462. Magnesium Sulphate in the Withdrawal of Alcohol and Its Complications. (Le sulfate de magnésie dans le sevrage alcoolique et ses complications)

N. PLANTE. *Laval médical* [Laval *méd.*] 31, 147-155, Feb., 1961. 13 refs.

Out of a diversity of treatments for alcoholism and the complications of withdrawal the author has chosen magnesium sulphate. He maintains that its value is due not to its effect upon cerebral oedema, but to its anticholinergic action at the motor end-plate which results in a diminution of agitation. As well as having a depressant effect upon the central nervous system magnesium sulphate acts like a local anaesthetic peripherally, cutting out afferent sensory stimuli at subcortical levels. The patient becomes calm and cooperative, is able to feed himself, and requires the addition of only small doses of sedatives for the restoration of a normal sleep rhythm. Furthermore, magnesium catalyses the utilization of glucose. The author has not observed any signs of toxicity or local reactions when the substance was given slowly intravenously. Neither the blood pressure nor respiration was affected, and the patients experienced only a diffuse feeling of warmth concentrated in the region of the upper chest, occasionally accompanied by a temporary feeling of constriction. The patient discovers an aversion for alcohol, spontaneously asks for water or fruit juice, and wants to eat. Sleep follows, tremors cease, and the suffusion gradually disappears.

Of 267 patients so treated at the Hôpital Saint-Michel-Archangel, Quebec, during a period of 18 months, most of them periodic drinkers, 120 were classified as suffering from acute alcoholism, 79 from chronic alcoholism, 30

from alcoholic psychoses, and 38 from a confusional state or delirium tremens; the mean age was 38 years. Alcohol was withdrawn immediately following admission and 6 to 8 g. of magnesium sulphate given in 3 or 4 intravenous infusions each of 10 ml. of a 20% solution over the 24 hours, one fewer infusion being given each subsequent day. For patients who were hyperpyretic, agitated, delirious, or dehydrated the infusion was followed by the administration of one litre of fluid containing a further 20 ml. of 20% magnesium sulphate, and if required a further 10 ml., making a total intake of 8 g. within 3 or 4 hours and 12 to 14 g. in the 24 hours. All patients were given a sedative at night, usually 3 grains (0.2 g.) of phenobarbitone and sometimes also "sparine" (promazine chloride). Within 36 hours the temperature was usually normal and the tremor and delirium were beginning to disappear. In 5 cases additional vitamin B was required because of sensory loss, while antibiotics were administered when there was an infection or when the patient's temperature was over 102° F. (38.9° C.). A further 7 patients addicted to barbiturates and one to pethidine, in addition to alcohol, were also satisfactorily weaned. The author stresses that smaller doses of magnesium are required when there is oliguria, and an excess of magnesium is recognized early by a diminution of the tendon reflexes; calcium gluconate is a satisfactory antidote. In this series of patients the mortality was *nil* and there were no complications. Magnesium lowers the raised intracellular potassium content which is present in delirium tremens. Although there may be a specific deficit of magnesium in chronic alcoholism, the author prefers to regard the beneficial effect of this drug as being more likely due to its curare-like and anaesthetic effects which produce an early tranquility.

J. S. Bearcroft

AFFECTIVE DISORDERS

463. Treatment of Depression with Imizin ("Tofranil"). (Лечение депрессий имизином (тофранилом)) T. N. MOROZOVA. *Журнал Невропатологии и Психиатрии* [Z. *Neuropat. Psihiat.*] 61, 176-182, No. 2, 1961. 10 refs.

Imizin is a preparation synthesized at the All-Union Chemico-pharmacological Institute corresponding in structure and action to "tofranal" (imipramine). At the Gannushkin Psychoneurological Institute No. 4 81 patients have been treated since 1959 with imizin. The best results were obtained in cases of manic-depressive psychosis in the depressive phase or cases of cyclothymic depression. Of 31 such patients, 17 were discharged in a good or satisfactory state, 3 developed agitation, and 2 had to have treatment suspended for somatic reactions, while 9 are still under treatment. The dose was 200 to 300 mg. every 24 hours and the duration of treatment averaged 2½ months. Two out of 3 patients with involutional depression also improved enough to be sent home. In one case of pre-senile depression convulsions developed, followed by obstinate insomnia. Whether this was due to imizin or to previous electric

convulsion therapy it is difficult to say. After the attack the patient's condition improved remarkably and she was discharged home. Four patients with organic brain disease (arteriosclerosis and post-meningo-encephalitic changes) associated with depression required cautious dosage owing to sensitivity to imizin, but their depression was relieved.

Altogether, 42 patients with schizophrenia of which depression was a feature were treated. Of 16 cases of depressive-paranoid schizophrenia, 2 are still under treatment. In this group depression was accompanied by fear, ideas of guilt, anticipation of his own death or that of his family, and a sense of unreality in the surroundings. These symptoms responded well to imizin, but were often replaced by ideas of persecution; when this happened imizin was given in combination with aminazine (chlorpromazine) with good effect. Four patients with depressive-paranoid psychosis improved as regards tidiness, interest in life, and capacity for work, though emotional frigidity remained; 6 were resistant to imizin. Of 16 patients with the same condition who developed suicidal tendencies while under treatment with chlorpromazine, these disappeared in 7 cases when imizin was substituted, but the rest were resistant.

Side-effects occurred in 53 out of 81 patients. These consisted in vertigo (11), dry throat and mouth (8), general weakness (7), tachycardia (6), nausea and vomiting (6), and sweating, insomnia, facial hyperaemia, loquacity, tremor, and retention of urine in individual cases. Two patients developed dermatitis. All these symptoms subsided on withdrawal of the drug, with or without antihistamine treatment. L. Firman-Edwards

464. The Influence of Blood from Patients with Manic-depressive Psychosis on the Behaviour of Animals. (Влияние крови больных маниакально-депрессивным психозом на высшую нервную деятельность (поведение) животных) M. JA. POLIAKOVA. *Журнал Невропатологии и Психиатрии* [Z. *Neuropat. Psihiat.*] 61, 104-108, No. 1, 1961. 1 fig.

Experiments are described in which the blood serum of patients with manic-depressive psychosis at various phases was injected into dogs which had previously been conditioned to finding their way through a labyrinth to obtain food. Ten patients in the manic phase and 13 in the depressive phase provided the blood. Five dogs were trained to pass through the labyrinth by the correct route until they made no mistakes in 20 successive journeys. They were rewarded on each occasion with a portion of meat and the time taken to perform the feat was noted. Then, after 10 ml. of serum from one of the patients had been injected intravenously into each dog, the test was repeated.

When serum from patients in the depressive phase was given the average time taken by each dog to perform the test was prolonged up to threefold, but the number of mistakes made was not increased. The dogs, however, were listless and tired after retesting, and this effect lasted for about 30 minutes. When serum from patients in the manic phase was given the average time taken for

the test was reduced in every case, but there were more mistakes and the dogs were restless for over half an hour. Administration of serum from healthy persons had no effect on the reaction of the dogs.

It therefore appears that the serum of such patients contains some substance which accelerates cerebral action in the manic phase and inhibits it in the depressive phase. One remarkable fact elicited was that the dogs with a stable nervous system showed more inhibition with depressive serum than the others, while those with a less stable type of nervous system made more mistakes and had a shorter reaction time with the serum of maniacal patients.

L. Firman-Edwards

SCHIZOPHRENIA

465. **Intellectual Level and Schizophrenia.** (Le niveau intellectuel et les schizophrénies)
P. LAB. *Encéphale* [Encéphale] 49, 544-556, Nov.-Dec., 1960 [received March, 1961]. 8 refs.

The author briefly reviews the literature on the relationship between schizophrenia and intellectual level and formulates three problems: (1) whether the distribution of intellectual level in a group of schizophrenics differs from that in other groups of patients; (2) whether there is any association between the classic clinical forms of schizophrenia and premorbid intellectual level; and (3) whether the intellectual level influences the natural course of the illness and the response to treatment. He then reports a study based on the case notes of 357 patients admitted to three psychiatric services during 1957-8. The patients were classified as definitely schizophrenic, definitely not schizophrenic, and of uncertain diagnosis. The schizophrenic group was further classified into hebephrenic, catatonic, paranoid, and *délire chronique*. Intellectual level, assessed by I.Q. tests where possible but mainly on educational records, was classed as high, intermediate, or low.

Of 151 definitely schizophrenic patients, 22% were found to be in the highest intellectual level compared with 7% of 119 definite non-schizophrenics. This difference may be largely a reflexion of bias in sampling, but the figures for each of the three services show that among patients of high intellectual level the number of schizophrenics exceeded that of non-schizophrenics, while among patients of the lowest intellectual level the reverse was true. Examination of school records showed that schizophrenic patients of high level had shown little evidence of educational disturbance and had apparently used their capacities to the maximum. Many schizophrenics of low level had shown evidence of gross disturbances in infancy and childhood. Among the schizophrenic group, hebephrenics were more often classed in the lowest intellectual level than in either of the higher levels; this pattern was different from that in patients with paranoid and catatonic illnesses, but the differences were not significant. There was evidence that age of onset of the illness (classed as above or below 26 years) was significantly lower in the hebephrenic and catatonic groups than in the paranoid group. Age of

onset was also related to intellectual level, being apparently earlier in patients of higher intellectual level. Of the 151 schizophrenic patients, 135 had illnesses with a progressive or remittent course. The remittent course was found more frequently in patients with low intellectual levels (16 out of 27) and the progressive course was more common in patients with higher intellectual levels (17 out of 33). Similarly, over-all response to treatment was best in the group of lowest intellectual level (42% good response) and worst in the group of highest level (15% good response).

The author concludes that there is evidence that (1) the schizophrenic population contains a higher proportion of patients of high intellectual levels and a lower proportion of low intellectual levels than other groups of psychiatric patients; (2) there is no significant association between the classic clinical forms of schizophrenia and intellectual level; and (3) high intellectual level is associated with earlier age of onset of illness and with a worse prognosis and less satisfactory response to treatment.

R. H. Cawley

TREATMENT

466. **The Use of Psychopharmacologic Agents in Retarded Children with Behavior Disorders**
G. D. LAVECK and P. BUCKLEY. *Journal of Chronic Diseases* [J. chron. Dis.] 13, 174-183, Feb., 1961. 19 refs.

This paper reviews the effects of 5 tranquillizing drugs on children with behaviour disorders at the Rainier School, Buckley, Washington. With the exception of one drug (mephenoaloxone) a double-blind technique was used, equal groups of children matched for age, sex, and intellectual ability being compared. [It is not stated whether the groups were matched for severity of disturbed behaviour.] Criteria are not given for the assessment of improvement; this was based on the observations of the nursing attendants.

Of 24 children given fluphenazine, 2 were "markedly improved" and 8 "improved". One child was "markedly improved" on the placebo and 4 "improved". It was noted that the most severely retarded children derived greatest benefit from fluphenazine. The initial dose of 0.5 mg. daily was increased up to 7.5 mg. daily as indicated by the occurrence of side-effects and the child's clinical response. Meprobamate, 200 mg., and promazine, 25 mg., were given in combination to 27 children, starting with one capsule 3 times a day and increasing as necessary. Although 11 of these children were improved compared with 4 of the controls, side-effects, particularly drowsiness, were very prominent and improved behaviour appeared to be related to drowsiness. Spasticity, intelligence, and motor ability were not improved. Deanol was given to 25 children in a dosage of 75 mg., later increased to 150 mg. daily; 9 of these were improved and 10 of the control group. Deanol was not found to improve attention, reaction time, or distractibility. Mephenoaloxone was given to 27 children, starting at 200 mg. every 12 hours and increasing to 400 mg. 3 times a day. There were no side-effects. There was no improvement in behaviour, but 2 out of 15 children

with spasticity were able to straighten previously "tight" extremities and some muscle relaxation occurred in a further 3. Chlordiazepoxide was given to 14 patients and a placebo to 14 others for 6 weeks, after which the groups were reversed. The dose given was 10 mg. 3 times a day for those weighing under 50 lb. (22.6 kg.) and 25 mg. 3 times a day for heavier patients. There was no improvement in behaviour, nor was there any reduction in the incidence of convulsions among epileptics; in fact, negative and undesirable behaviour tended to increase.

The authors note that these findings do not support previous enthusiastic reports on the various drugs. They point out the difficulties of assessing changes in disturbed behaviour and stress the need for very careful evaluation of new treatments offered for disturbed and retarded children.

Christopher Wardle

467. The Use of LSD-25 in the Treatment of Alcoholism and Other Psychiatric Problems

J. R. MACLEAN, D. C. MACDONALD, U. P. BYRNE, and A. M. HUBBARD. *Quarterly Journal of Studies on Alcohol* [Quart. J. Stud. Alcohol] 22, 34-45, March, 1961. 4 refs.

This paper from the Hollywood Hospital, New Westminster, Canada, describes the treatment of alcoholics and other psychiatric patients with one large dose of D-lysergic acid diethylamide (LSD-25) given in a group setting. The actual procedure and the atmosphere in which the drug is given are described in detail, as these are held to be of great importance. After 2 days of psychiatric assessment 400 to 1,500 µg. of LSD-25 is given to the patient by mouth in a group consisting of the therapist, a psychologist, a nurse, and a music therapist. Eight hours after ingestion of the drug the patient returns to his room, where a therapist remains with him for several hours. The patient is discharged the following day.

The authors treated 61 alcoholics and 39 other patients by this method and followed them up for periods ranging from 3 to 18 months, when it was found that 30 of the alcoholics and 22 of the other patients were much improved. The authors claim that this single overwhelming psycholytic experience is effective in some alcoholics. A few case histories are presented and theoretical considerations discussed, while the therapeutic milieu is particularly emphasized.

B. M. Davies

468. Comparative Clinical Study of the Effects of Disulfiram and Calcium Carbimide. II. Reaction to Alcohol

J. MARCONI, G. SOLARI, and S. GAETE. *Quarterly Journal of Studies on Alcohol* [Quart. J. Stud. Alcohol] 22, 46-51, March, 1961. 7 refs.

This report from the Psychiatric Clinic of the University of Chile, Santiago, compares the response to alcohol of patients receiving disulfiram ("antabuse"), calcium carbimide, and a placebo. The tests were carried out by the double-blind technique on 23 alcoholic men under the age of 50. One group of 12 received calcium carbimide for 20 days, then a placebo for 20 days, then

disulfiram for 20 days, while the remaining 11 received the drugs in the reverse order for 20 days each. An alcohol test was made on each patient during each period of the trial.

A strong reaction occurred on each occasion with disulfiram, on 20 out of 23 occasions with calcium carbimide, and on 7 with the placebo. The reaction to alcohol during treatment with calcium carbimide was less severe than with disulfiram—in particular cyanosis and chest pain were less common and less severe. However, the symptoms that did occur with calcium carbimide were considered to be sufficient to discourage further ingestion of alcohol by the patient.

B. M. Davies

469. Ditrán, a Psychotherapeutic Advance: a Review of One Hundred and Three Cases

B. A. FINKELSTEIN. *Journal of Neuropsychiatry* [J. Neuropsychiat.] 2, 144-148, Feb., 1961. 6 refs.

The use of lysergic acid diethylamide (LSD) as an aid to psychotherapy in the treatment of patients with long-standing, intractable psychoneurotic illnesses is now fairly well established. The author reports his experience at Eastern State Hospital, Lexington, Kentucky, with another psycholytic drug, "ditran", used in the same way as LSD. Each 15 mg. of ditran contains 12.5 mg. of N-ethyl-1-pyrrolidyl-methylphenylcyclopentyl glycolate hydrochloride and 4.5 mg. of N-ethyl-3-piperidylphenylcyclopentyl glycolate hydrochloride and is given by intramuscular injection. It produces hallucinations as does LSD, but the affective changes are less severe; however, they persist for several days, making it necessary to restrict its use to hospital practice. Electric convulsion therapy was also given to 27 of the patients receiving ditran. Of the 103 patients treated, 89 improved, 17 of them showing a complete remission of symptoms.

B. M. Davies

470. One Year's Experience with Trifluoperazine in Treatment of Chronic Mental Disorders

V. S. ALLEN. *Journal of Clinical and Experimental Psychopathology* [J. clin. exp. Psychopath.] 21, 285-292, Oct.-Dec., 1960 [received March, 1961]. 4 refs.

Encouraged by earlier results (*J. clin. exp. Psychopath.*, 1959, 20, 247), the author has continued the trial of trifluoperazine in chronic schizophrenic patients, extending it to the treatment of patients with other chronic mental disorders, all of whom had been refractory to previous treatment.

Included in the trial were 57 withdrawn and deteriorated schizophrenics, ill for 7 to 12 years, who were treated with 10 to 40 mg. of trifluoperazine daily. Improvement, based on symptomatic and behavioural criteria, was rated as marked, moderate, or minimum at intervals of 3, 6, and 12 months. After a year's treatment 48% of the patients showed marked improvement and could be given week-end passes and leaves of absence. Commenting on the use of trifluoperazine in such cases the author advocates that the dose should be gradually increased to 30 to 40 mg. daily, kept there for 3 to 4 months, and then reduced to a maintenance level of 10 to 20 mg. a day. It is emphasized that successful drug

treatment must form part of a full therapeutic programme.

Twenty patients with chronic anxiety reactions who had required frequent readmission to hospital over the previous 8 or 9 years were treated with 4 to 20 mg. of trifluoperazine daily for 4 to 5 months, the dose then being reduced to 4 to 5 mg. daily. After 3 months' treatment 80% were improved in their ability to accept and to cooperate in psychotherapy and 62% were able to return home and to start work.

Also included were 10 geriatric patients with chronic brain syndrome associated with senility or cerebral arteriosclerosis who had been in-patients for at least 15 years. Most were hallucinated, deluded, and apathetic, and treatment was initiated with the hope of reducing problems of ward management. Trifluoperazine was started in a dose of 4 mg. a day, gradually increased to 10 mg. a day, and then reduced to a daily maintenance dose of 4 to 5 mg.; benzotropine methanesulphonate was given concomitantly. All patients showed improvement and, because of better cooperation, 6 of them who had been difficult to feed gained weight.

Side-effects were avoided by gradual adjustment of dosage and by dealing promptly with extrapyramidal symptoms. No severe clinical abnormalities were encountered, and the only laboratory finding of note was a mild leucocytosis with a normal differential count.

[It is hoped that adequate follow-up studies will be made available.]

Alan A. Black

471. A Controlled Trial of "Gerioptil"

M. D. CASHMAN and T. G. G. LAWES. *British Medical Journal* [Brit. med. J.] 1, 554-556, Feb. 25, 1961. 11 refs.

"Gerioptil" contains procaine together with a variety of vitamins and vitamin derivatives and is equivalent to the "Compound H3" of Aslan. The authors, noting criticism of the claims made by Aslan for H3, designed a small double-blind trial upon 12 elderly women with senile or arteriosclerotic dementia. Memory and learning abilities were tested by forms of the Wechsler memory scale, with subtests. Ability to perceive and reproduce visual patterns was assessed by the Bender gestalt test, intellectual capacity by Raven's Progressive Matrices, and premorbid intelligence by the Mill Hill vocabulary definitions. After one month's treatment with 12 intramuscular injections, 6 of the patients receiving gerioptil and 6 sterile water, all the subjects were retested. Four of the 6 treated patients were found to have deteriorated, yet 5 of the 6 untreated patients had improved. In all the individual tests except that of memory for design no benefit was derived from the course of gerioptil: rather, the evidence from this admittedly small series is that the preparation had an adverse effect.

J. N. Agate

472. Results of Lobotomy

W. I. TUCKER. *Journal of Neuropsychiatry* [J. Neuropsychiat.] 2, 153-157, Feb., 1961. 5 refs.

The results of lobotomy in 132 patients operated on at the Lahey Clinic, Boston, between 1946 and 1958 are reported. Bilateral prefrontal lobotomy was performed

until 1949, when bimedial prefrontal lobotomy took its place. The various diagnostic categories included depression, obsessive-compulsive psychosis, schizophrenia, and intractable pain. The follow-up period ranged from over 6 months to 12 years. In 28 of 37 depressed patients the results were good, as they were in 14 of 22 obsessional patients. In 13 of 25 schizophrenic patients the results were poor. In cases of intractable pain the results were generally good.

These results are discussed and positive indications for the operation laid down as follows. (1) Symptoms of agitation, depression, self-concern (obsession or intractable pain), should be present. (2) The condition should be such that it could not be expected to respond to any other type of treatment. (3) The degree of suffering and incapacity must be sufficient to justify the operation. (4) The family situation should be favourable for rehabilitation of the patient. (5) The expected post-operative condition must be considered a sufficient improvement to justify the operation. (6) There should be no organic brain disease."

B. M. Davies

473. Longitudinal Studies with Rorschach and Szondi Tests of Depressive Illness Treated with Electric Convulsion Therapy. (Längsschnittuntersuchung elektrochock-behandelter melancholischer Phasen im Rorschach- und Szondi-Versuch)

T. KOHLMANN, H. OSWALD, and H. GASTAGER. *Wiener Zeitschrift für Nervenheilkunde und deren Grenzgebiete* [Wien. Z. Nervenheilk.] 18, 263-283, 1961. 22 figs., 19 refs.

The Rorschach and Szondi tests were performed before and after treatment with electric convulsion therapy (E.C.T.) on 50 female patients admitted to the Psychiatric and Neurological Clinic of the University of Vienna with a diagnosis of endogenous depression. It was found that the Rorschach test, unlike the Szondi test, was capable of demonstrating improvement after E.C.T. objectively. The main indication of improvement was an increase in colour response. In uncomplicated cases of endogenous depression there was good correspondence between the test result and the clinical assessment. Where there were neurotic features the improvement shown by the Rorschach test was less than that assessed clinically. So far as prognosis was concerned the patients with pure endogenous depression showed a good remission both on the basis of the test and clinically, whereas those with neurotic features showed only slight or no improvement after the control period of 14 days and early remissions were frequent. This was attributed to a neurotic fixation of the depressive picture. A similarly poor prognosis was shown by patients with cerebral arteriosclerosis or other organic lesions. The use of additional therapeutic measures such as psychotherapy, social care, or "antisclerotic medication" were of great help in producing early recovery. J. Hoenig

474. Cardiovascular Aspects of Electric Shock Therapy. [Monograph, in English]

G. M. PERRIN. *Acta psychiatrica et neurologica Scandinavica* [Acta psychiat. scand.] 36, Suppl. 152, 1-45, 1961. 4 figs., bibliography.

Dermatology

475. Intralesional Injections of Triamcinolone Acetonide; a Therapy for Dermatoses

A. HOLLANDER. *Antibiotic Medicine and Clinical Therapy* [Antibiot. Med.] 8, 78-83, Feb. [received April], 1961. 5 refs.

The author describes the results of intralesional injections of a sterile aqueous suspension of triamcinolone acetonide in 230 patients with various dermatoses. From 0.2 to 3 ml. of the suspension was given at each injection according to the size of the lesion, care being taken that the whole of the lesion was infiltrated. An average of 2 to 3 injections per lesion proved adequate.

Response graded as "excellent" was obtained in most cases of chronic eczematous conditions, many cases of lichen simplex chronicus showing no recurrence after 18 months; some other forms, such as dyshidrotic eczema, did recur, however. All cases of acute dermatitis with lesions confined to the head and upper body healed within one to 2 weeks. Localized patches of psoriasis healed generally, but tended to recur. Repeated injections controlled vesico-pustular eruptions on the hands and feet and re-established hair growth in alopecia areata. Satisfactory results were also obtained in cases of keloid (only those of fairly short duration were treated), granuloma annulare, and localized lichen planus. One case each of benign mucous-membrane pemphigus and pemphigus erythematous, after successful treatment, were effectively maintained on this therapy.

Side-effects included prolonged menstrual bleeding in 6 women; normal menstrual cycles were, however, re-established upon cessation of treatment. Whitish macular atrophy developed in a number of cases, disappearing generally in a few weeks or months, but persistent in some cases. No systemic side-effects were recorded.

The author considers that further investigations into the mode of action, possible tissue damage, and overall and lasting value of this type of treatment are required.

G. B. Mitchell-Heggs

476. Leg Ulcers: Assessment of Response to Certain Topical Medicaments

A. G. FERGUSSON and J. C. P. LOGAN. *British Medical Journal* [Brit. med. J.] 1, 871-874, March 25, 1961.

In order to compare the efficacy of various forms of treatment the authors have studied the clinical course of healing of 343 leg ulcers in 271 patients (183 females, 88 males) seen at Stobhill General Hospital, Glasgow, during the past 10 years. The patients' ages ranged from 17 to 84 years. Some of the ulcers had been present for as long as 20 years. Of the ulcers, 96% were gravitational, 1% trophic, and 3% ischaemic in origin. As bases for comparison the rate of healing was determined by regular measurement of the ulcer with the aid of tracing paper and the proportion of ulcers which healed with each type of treatment was calculated. The medicaments were applied twice a day.

Eusol (1:4), used on a total of 71 ulcers, achieved a mean rate of healing of 61.4 sq.mm. a day, while 95.6% healed completely. Simple pastes containing 1% eosin, 1% ichthylol, 1% gentian violet and 1% brilliant green, 1% salicylic acid, 10% balsam of Peru, 1% boric acid, or talc and kaolin, used on 21 ulcers, produced almost the same percentage of healing, but a slower rate (52.2 sq.mm. a day). Ichthylol calamine liniment (74 ulcers) produced 97.3% cures at a rate of 49 sq.mm. a day, while with 20% zinc peroxide triturated with water (77 ulcers) cures were obtained in every case, but at a mean rate of only 33.7 sq.mm. a day. Topical ointments containing various antibiotics, used on 10 ulcers, were comparatively slow in healing (31.3 sq.mm. a day) and resulted in healing only 7 (70%) of ulcers. Simple saline applications (8 ulcers) were successful in 87.5%, but at the remarkably slow rate of 20.0 sq.mm. a day. Petroleum jellies (including tulle gras) (9 ulcers), "gelfoam" (25), antiseptics (16), and triiodothyronine (15) all had very slow rates of healing (20 to 40 sq.mm. a day), with complete healing in 66.7 to 100% of cases. Nitrofurazone (17 ulcers), although in general quite good, produced sensitivity reactions in 25% of cases.

From their experience in these cases the authors conclude that simple diluted eusol is the best available therapeutic agent for leg ulcers, though its use must be combined with adequate recumbency, and that micro-organismal activity is of little importance in causing chronicity. Finally a plea is made for more investigation into the mechanism of leg ulceration, about which no major progress has been made since Anning's work on preceding venous thrombosis.

Allene Scott

477. Griseofulvin Therapy in Tinea Capitis

J. ALBAN. *Journal of Pediatrics* [J. Pediat.] 58, 367-372, March, 1961. 5 figs., 9 refs.

The results of the treatment of tinea capitis due to *Microsporum audouinii* (52 cases) or *M. Canis* (6 cases) with oral griseofulvin are reported from Johns Hopkins University School of Medicine, Baltimore. The 58 patients (46 girls) ranged in age from 1 to 12 years. Dosage varied, according to age and severity, between 250 mg. twice daily and 500 mg. four times daily. A case was considered cured when there was no fluorescence under Wood's light or after 2 negative cultures.

Cure was obtained in 2 cases in less than 3 weeks, and eventually all were cured, though in 14 cases more than 11 weeks' treatment was required. Transient rashes occurred in 2 cases, but cleared up with antihistamine therapy and did not recur when administration of griseofulvin was resumed. There were 9 cases of leucopenia, with a leucocyte count below 5,000 per c.mm., but in all these the count rebounded without interruption of treatment. One case, in which the leucocyte count fell below 3,000 per c.mm., is described in some detail; the cell count rapidly became normal when the drug was

withdrawn, by which time, fortunately, the infection was practically cured. Nevertheless, a further course of griseofulvin was given under close observation, but after 5 days the count again fell and once more griseofulvin was discontinued, whereupon recovery was complete and rapid. This was the only serious toxic reaction in the series.

E. H. Johnson

478. Further Observations on the Bacteriology of Impetigo and Pemphigus Neonatorum. [In English]

M. T. PARKER and R. E. O. WILLIAMS. *Acta paediatrica [Acta paediat. (Uppsala)]* 50, 101-112, March, 1961. 2 figs., 25 refs.

The authors describe a bacteriological study of the lesions from 609 cases of impetigo which occurred between 1953 and 1957 in the Manchester area. This showed that 47% of the cases were due to staphylococcal infection, 21% to streptococcal infection, and 11% to a mixture of these two; no pathogen was isolated in the remaining 21%. Of the 514 cases in school-children in Salford, over one-fifth were streptococcal, whereas of the 95 cases seen at a hospital clinic, nearly all (97%) were staphylococcal. During 1953, when the incidence was at its highest, *Staphylococcus aureus* Type 71 was isolated in 70% of the staphylococcal cases, but this proportion had fallen to 47% by 1957. Most of the streptococcal cases were due to one of two strains of *Streptococcus pyogenes*, these two strains being equally prominent in the cases of mixed infection, whereas the proportion of *Staph. aureus* Type 71 was lower in the mixed infections than in the "pure" infections. It is suggested that the impetigo caused by *Staph. aureus* Type 71 is a more severe bullous skin infection, while that due to *Str. pyogenes* is a milder infection rarely seen in hospital clinics.

Of 34 outbreaks and 17 sporadic cases of skin sepsis in the newborn, *Staph. aureus* Type 71 was found in 54%. These cases, most of which were seen in hospital although a few occurred in domiciliary practice, were of all grades of severity ranging from a mild eruption to pemphigus neonatorum. The characteristic lesion in infections due to Type 71 was a superficial blister with little surrounding inflammation. The outbreaks were usually small, comprising only a few cases. One such outbreak in a village is described; it involved 2 cases of exfoliative dermatitis (one fatal) and one of impetigo in newborn infants, and *Staph. aureus* Type 71 was isolated from the skin lesion of one of the infants and from the nose of the midwife attending the births.

E. H. Johnson

479. Studies in Contact Dermatitis. XI. Copy Paper Dermatitis

R. R. M. HARMAN and I. SARKANY. *Transactions of the St John's Hospital Dermatological Society [Trans. St John's Hosp. derm. Soc. (Lond.)]* No. 44, 37-42, 1960 [received April, 1961]. 10 refs.

Four methods of reproducing (copying) original manuscripts and drawings are used commercially today: (1) photocopying, in which a photosensitized paper, often incorporating a developer and fixer, is exposed to the image of the original document in the path of light (the

"verifax" process is of this type); (2) the dyeline or diazo process, in which a fluorescent light transmits the image on to a diazo-sensitized paper which is then developed with ammonia (this method is limited to drawing offices); (3) a heat process in which a catechol-sensitized paper is exposed to heat ("thermofax" method); and (4) the electrostatic process, with an inert paper, an intermediary such as selenium, and a chemically inert, fully-polymerized resin for delineating the image.

The authors of this paper from King's College Hospital, London, describe 5 patients who developed a sensitivity to copy paper during either the process of manufacture or its use in an office. None of the cases arose out of Process 4, but it was found that the 4-phenylcatechol used for impregnating the paper in the verifax process frequently gave trouble during manufacture. It is interesting that this chemical is related to the sensitizing catechols found in American poison ivy. Thermofax, on the other hand, in which a catechol is also used, caused contact dermatitis in office users. The manufacturers of thermofax have recently introduced a new "spiro" resin (chemical formula not yet available), which may possibly remove the danger of sensitization. Only one of the patients was found to be sensitive to ammonia as used in Process 2.

Allene Scott

480. Erythema Nodosum

D. G. JAMES. *British Medical Journal [Brit. med. J.]* 1, 853-857, March 25, 1961. 5 figs., 7 refs.

Collected by the author between the years 1950 and 1959, 170 cases of erythema nodosum, predominantly in adults, have been investigated with particular regard to aetiology. The general pattern demonstrated a spring incidence, a female preponderance (3:1), and a maximum frequency in the age group 20 to 29 years. Lesions on the arms were present in 7% of cases, while all the patients developed lesions on the legs. There was no deviation from the clinical description originally propounded by Willan in 1808, although many patients had constitutional signs such as fever for a few days before the eruption, and 62% had varying degrees of polyarthralgia. Radiographs, Mantoux and depot tuberculin tests, the Kveim test, electrophoresis of the serum proteins, and estimations of the erythrocyte sedimentation rate and serum antistreptolysin titres demonstrated that in 74% of cases the outbreak was associated with clinical or laboratory signs of definitive sarcoidosis, and a similar aetiology was likely in a further 9%, although the strict criteria set forbade definite inclusion in the group. In 13% of cases the lesions developed in association with infection (streptococcal in 12 cases, tuberculous in 4, pneumonia in 3, and acute colitis and dental abscess in one each). In the remaining 4% investigation failed to reveal a possible cause.

It was felt that the use of the Kveim test offered the best opportunity of establishing an aetiological diagnosis. The lesions of erythema nodosum usually clear rapidly without treatment within 6 weeks, although in a few cases in this series they persisted for as long as 20 weeks. Recurrences were infrequent, occurring only in 8%, and usually within 3 months. The radiographic and other

manifestations of sarcoidosis cleared completely, usually in 6 months, although a few were prolonged as long as 6 years. Only one patient with iridocyclitis suffered lasting damage from the attack. In view of the excellent results the use of steroids, which might interfere with a little-known immune reaction, is not indicated in treatment.

Allene Scott

481. Blood Lipids in Psoriasis. The Effects of "Lipostabil"

J. B. ENTICKNAP, C. C. RYAN, and T. S. LANSLEY. *British Journal of Dermatology* [Brit. J. Derm.] 73, 99-102, March, 1961. 9 refs.

Stating that it has been reported that "dietary deficiency of certain polyunsaturated fatty acids results in skin changes in rats not unlike those seen in human psoriasis" the authors describe a trial of these fatty acids in the treatment of 6 women with psoriasis, 6 others who received a placebo forming a control group. Most of the patients were given daily 6 capsules containing 320 mg. of soya bean extract and 0.6 mg. of pyridoxine, with 0.1 mg. of α -tocopherol as an anti-oxidant; for the control group the placebo capsule contained lactose and α -tocopherol. The serum lipid content and lipid fractions were fully investigated before treatment, after a fast of 12 hours, and periodically during 3 months' observation. There was no significant difference between the two groups, no clinical response to the treatment, and the serum lipid levels, which were initially normal, did not change during or after the treatment.

S. T. Anning

482. Oral Steroid Therapy in Psoriasis Vulgaris. A Comparison of Triamcinolone, Methyl Prednisolone and Dexamethasone

C. W. MARSDEN. *British Journal of Dermatology* [Brit. J. Derm.] 73, 103-106, March, 1961. 1 fig., 35 refs.

At the Manchester and Salford Hospital for Skin Diseases 30 selected patients with extensive psoriasis were given either triamcinolone (4 mg.), or methyl prednisolone (4 mg.), or dexamethasone (0.5 mg.) 3 times daily for one week, twice daily for 2 weeks, and once daily for a further 3 weeks. The trial was "blind" and each group of 10 patients was allotted to a particular steroid by means of random numbers. Triamcinolone proved to be the most effective of the three drugs employed, producing a remission in 6 out of 10 patients, of whom 2 remained clear of lesions or greatly improved for 3 months and 2 for 2 months. Although there was a gradual relapse the patients' condition still remained much better than before steroid therapy. [The statistical significance of the results, however, is not estimated.]

S. T. Anning

483. Intraleisional Triamcinolone Acetonide in the Treatment of Psoriasis

M. D. READETT. *British Journal of Dermatology* [Brit. J. Derm.] 73, 107-109, March, 1961. 8 refs.

At the Royal Infirmary, Liverpool, 11 patients with psoriasis were treated by intraleisional injections (subcutaneous in 4 cases) of triamcinolone acetonide solution containing 5 or 6 mg. per ml. Patches of psoriasis were

infiltrated with the solution; in all cases these lesions cleared within 10 to 17 days and no relapse occurred during a follow-up period varying from 3 to 6 months. The author states that although the results are encouraging, the usefulness of this form of treatment is limited, but nevertheless a more extensive trial appears to be warranted.

S. T. Anning

484. Histochemical Changes in Psoriasis Treated with Triamcinolone

A. JARRETT and K. M. WITHAM. *British Journal of Dermatology* [Brit. J. Derm.] 73, 110-119, March, 1961. 1 fig., 8 refs.

The authors describe the histological and histochemical changes observed in 3 patients with psoriasis who were given triamcinolone in a dose of 4 mg. by mouth twice daily. In one the psoriasis cleared within 43 days and another showed great improvement in 34 days, but the third showed no improvement after 49 days' treatment.

Biopsies were performed before treatment started and several times during the period of administration of triamcinolone. The biopsy specimens were examined histologically by routine methods, by fluorescent techniques, and by certain histochemical methods. It was found that a granular layer was rapidly reformed during the remission induced by triamcinolone, but in the epidermal cells the cytoplasmic content of ribonucleic acid remained high even after complete recovery. The significance of these findings is discussed.

S. T. Anning

485. "Bralium" in the Treatment of Psoriasis. [In English]

T. PASIECZNY and J. O'D. ALEXANDER. *Dermatologica* [Dermatologica (Basel)] 122, 1-5, Jan. [received March], 1961. 3 refs.

The authors, at the Royal Infirmary, Glasgow, have treated a group of psoriatic patients with "bralium", described by the manufacturers as "preparatio hydrargyri oleosa composita", and have compared the results with those in 2 other parallel groups treated respectively with maize oil and a routine form of therapy in use at the hospital. Bralium was supplied as an oily suspension in 5 strengths from 0.5% to 5%. All patients began with the lowest strength, the concentration being increased every 2 weeks according to tolerance.

In the controlled trial 9 out of 18 cases treated with bralium were cleared of all lesions compared with 3 cleared and 3 greatly improved out of 14 cases treated with maize oil and 3 cleared and 3 greatly improved out of 11 given routine therapy. A number of patients in whom other treatment failed were also treated with bralium, making a total of 30, and of these 18 (60%) were cured or greatly improved. Three cases relapsed when treatment was stopped, but improved again when it was resumed. The only side-effect noted was irritation in 5 cases, in only 2 of which did treatment have to be discontinued on this account. Several previously intractable cases responded well, as did scalp lesions generally. It is concluded that bralium is an aesthetically acceptable product which can readily be used in the patient's home.

G. B. Mitchell-Heggs

Paediatrics

NEONATAL DISORDERS AND PREMATURITY

486. Epidemic Meningitis of the Newborn Caused by *Flavobacteria*. I. Epidemiology and Bacteriology

H. A. CABRERA and G. H. DAVIS. *American Journal of Diseases of Children* [Amer. J. Dis. Child.] 101, 289-295, March, 1961. 2 figs., 8 refs.

In a period of just under 2 months 14 cases of meningitis occurred in a lying-in hospital in Columbus, Ohio. The offending organism in each case was found to be *Flavobacterium meningosepticum*, a long, pleomorphic, Gram-negative bacillus which grows well on blood plates. The illness affected mostly weak and newborn infants and resulted in a very high mortality (10 deaths). Extensive bacteriological investigations, involving well over 5,000 cultures, were undertaken. Nasal colonization was detected in 30 apparently unaffected infants, but no bacteriological carriers were identified among the nursery personnel. Bacteriological studies of the environment disclosed contamination with this organism of a faulty trap in one of the sinks in the premature infants' nursery. Repair of this trap brought the outbreak under prompt control.

[A bacteriological and epidemiological "whodunit".]

John Lorber

487. Epidemic Meningitis of the Newborn Caused by *Flavobacteria*. II. Clinical Manifestations and Treatment

R. M. GEORGE, C. P. COCHRAN, and W. E. WHEELER. *American Journal of Diseases of Children* [Amer. J. Dis. Child.] 101, 296-304, March, 1961. 1 fig., 4 refs.

This account of the clinical aspects of the outbreak of epidemic meningitis reported by Cabrera and Davis [see Abstract 486] is presented from the Children's Hospital, Columbus, Ohio, to which 12 of the 14 affected infants were admitted. The septicaemia or meningitis, or both, which occurred in these infants was shown to be due to *Flavobacterium meningosepticum*, but the symptoms were the same as those in newborn infants with sepsis and meningitis due to other bacteria. Only 2 of the 14 patients developed their first symptoms after the 5th day. The portal of entry was considered to be the nasopharynx. Of the 14 infants, 3 who received no antibiotic treatment died rapidly before the meningitis was recognized, while 5 others developed necrotizing meningitis which proved fatal in spite of early and vigorous antimicrobial therapy. Another 4 infants survived the meningitis but developed hydrocephalus, and one of them died later. The 13th infant, who had a positive blood culture but sterile spinal fluid, survived after treatment with erythromycin, and recovery in this case was complete. The 14th patient received only a very short course of vancomycin and although he survived he was left with gross hydrocephalus.

The findings in the spinal fluid were consistent with any type of pyogenic meningitis, an overwhelming number of organisms often being detected on direct smear. Sensitivity tests by the filter paper disk technique showed that, unlike other Gram-negative bacteria, *Flavobacterium meningosepticum* was sensitive only to erythromycin, oleandomycin, ristocetin, and vancomycin, and only the last two exhibited a bactericidal effect. On the whole, treatment gave poor results. Erythromycin intravenously, even in a dosage of up to 400 mg. per kg. body weight daily, was useless, and the organism became completely resistant to the drug within several days. Vancomycin was given intravenously in a dosage of 25 to 150 mg. per kg. daily, together with daily intrathecal administration (15 to 20 mg.). Of 6 patients treated with vancomycin, 4 survived. The survivors developed agglutinating antibodies against the infecting organisms.

John Lorber

488. "Enclosed" Hemorrhage and Neonatal Jaundice A. R. RAUSEN and L. K. DIAMOND. *American Journal of Diseases of Children* [Amer. J. Dis. Child.] 101, 164-169, Feb., 1961. 5 figs., 13 refs.

In this paper from the Children's Hospital Medical Center, Boston, the authors draw attention to the importance of haemorrhage into the tissues as a cause of potentially dangerous neonatal hyperbilirubinaemia and describe 3 such cases.

The first was in an Rh-positive infant weighing 2,295 g. who, following forceps delivery, showed bilateral cephalohaematoma and extensive superficial bruising. Vitamin K (5 mg.) was given intramuscularly. Jaundice appeared on the 3rd day. By the 4th there was a modest fall in the haemoglobin level and the serum indirect bilirubin level had risen to 20 mg. per 100 ml. Following an exchange transfusion the bilirubin level remained just below 20 mg. per 100 ml. for 3 days and then began to fall. Subsequent progress was satisfactory. The second infant, who weighed only 1,330 g. at birth, showed extensive bruising of the lower limbs. An exchange transfusion was required on the 4th day, when the indirect serum bilirubin level had risen to 20 mg. per 100 ml. and the haemoglobin level had fallen significantly; thereafter further progress was uneventful. In the 3rd case the child was mature, but showed extensive cutaneous haemorrhages following forceps extraction and a haemoperitoneum was suspected. Because of a marked thrombocytopenia, possibly due to placental venous thrombosis, an exchange transfusion of fresh blood was performed 11 hours after birth. By the 3rd day the serum total bilirubin value had risen to 18.8 mg. per 100 ml. but subsequently fell rapidly, and the infant was discharged on the 11th day.

The authors review the various factors known to produce hyperbilirubinaemia in the newborn and, although 2 of their patients were premature, they conclude that

breakdown of the blood sequestered in the tissues made a significant contribution to the high bilirubin levels observed. They stress that exchange transfusion is still the only effective way of treating patients in whom the serum indirect bilirubin level becomes dangerously high.

E. G. Hall

489. Staphylococcal Infection of the Newborn in Hospital and in Domiciliary Practice

T. F. ELIAS-JONES, I. GORDON, and L. WHITTAKER. *Lancet* [*Lancet*] 1, 571-574, March 18, 1961. 20 refs.

An investigation designed to compare the hazards of staphylococcal infection in newborn infants in hospital and domiciliary practice was carried out at Ilford, Essex, a borough with a population of 180,000, on the basis of information collected by 18 health visitors between July, 1957, and June, 1958. The health visitor paid a domiciliary visit about 3 weeks after the birth of an infant, whether this took place at home or in hospital, to assess the presence or absence of infection. When an infant showed signs of infection swabs were taken from various sites, and these were tested for staphylococci, any isolated being tested for sensitivity to antibiotics.

In all, 1,551 infants (70.8% of the available infant population) were visited. Of 1,129 infants born in hospital, 154 (13.6%) had septic lesions, the comparable figure for those born at home being 20 (4.8%) out of 414. (Eight nursing-home births were not included.) These differences are regarded as highly significant. Sepsis was significantly more prevalent in male infants. There were no seasonal fluctuations, nor did social conditions or antecedent obstetric complications influence the infection rates. The infections seen were mainly of a minor nature and involved predominantly the eyes, skin, and umbilicus (in that order of frequency). Pathogenic staphylococci were isolated from 77.5% of infants with clinical infection. Tests on apparently healthy infants showed a 50% staphylococcal carrier rate. Among infants born in hospital, 71% of those swabbed harboured pathogenic staphylococci, the rate for those born at home being 40.5%.

It is concluded that colonization by pathogenic staphylococci can be expected to occur in one out of every 2 babies by the age of 2 to 3 weeks. Those born in hospital run a much greater risk of acquiring virulent strains; in this survey no less than 90% of all antibiotic-resistant strains were isolated from such infants.

John Fry

490. Studies on the Effects of Human Growth Hormone in Premature Infants

J. R. DUCHARME and M. M. GRUMBACH. *Journal of Clinical Investigation* [*J. clin. Invest.*] 40, 243-252, Feb., 1961. 4 figs., bibliography.

In this paper from the College of Physicians and Surgeons, Columbia University, and the Babies Hospital, New York, the authors report a study of the effect of a purified preparation of human growth hormone on the immature infant in an attempt to elucidate the relation of this hormone to foetal and neonatal body growth. Five healthy premature infants weighing between 1,500 and 1,600 g. and aged approximately 2 weeks were given

a standard artificial feed 3-hourly which provided 120 Calories per kg. body weight per day. The human growth hormone was prepared from pituitary glands obtained at necropsy and was injected intramuscularly in total doses varying up to 30 mg. variously divided; no local or systemic reactions were observed. The periods of study were the week before, the week during, and the week after administration of the hormone. A comparable group of 7 untreated infants were studied during the same time to serve as controls.

It was found that the treatment resulted in no significant increase in rate of gain in weight or head circumference or of growth of the fibula, although one infant, who received the largest dose, 10 mg. a day for 3 days, showed an increase in fibula length which was significantly greater than that in the control group. A rise in blood sugar level and in the concentration of serum inorganic phosphorus was observed in the treated infants together with a fall in the blood urea nitrogen level. The intravenous injection of 1.25 mg. of growth hormone in 2 [? additional] cases did not add to the increased plasma concentration of free fatty acids obtained by fasting for 4 hours. It was not possible to affect the suppression of growth induced in one [additional] subject with ACTH (corticotrophin) by administering growth hormone concurrently. The serum levels of growth hormone in 5 premature infants [presumably untreated] were found to be within the range previously observed in older infants and children (230 to 480 mμg. per ml.).

The authors conclude that this preparation of growth hormone administered intramuscularly produces little response in the premature infant.

J. Warwick Buckler

CLINICAL PAEDIATRICS

491. The Incidence of Mental and Physical Handicaps in School-age Children of Very Low Birth Weight

C. M. DRILLIEN. *Pediatrics* [*Pediatrics*] 27, 452-464, March, 1961. 3 figs., 11 refs.

This most recent paper in the author's series of valuable follow-up studies of premature babies in Edinburgh [see *Arch. Dis. Childh.*, 1961, 36, 1; *Abstr. Wld Med.*, 1961, 30, 70] is concerned with 49 children whose birth weight was 3 lb. (1,360 g.) or less, born in 2 Edinburgh hospitals between 1948 and 1960, and now aged 5 years or older. The data provided include information concerning educational attainment, school behaviour, and physical defects.

Approximately one-half of these children were ineducable at a normal school because of physical or mental handicaps or both, one-quarter were dull children requiring special education, and one-quarter were of low average, average, or superior ability. One or more physical defects were present in 26 (53%) and 38 (78%) had behaviour problems. Of 30 with siblings for comparison, 22 were relatively retarded. In 5 of 7 pairs of twins the larger twin scored higher in intelligence tests than the smaller one. There was a significantly higher incidence of handicaps in children from the poorest homes. The

incidence of severe handicaps was significantly greater among children born between 1953 and 1954 than in those born in 1948 to 1950. This is in accordance with the view that the proportion of handicapped children is increasing, in this case owing to the increasing number of damaged children surviving. R. S. Illingworth

492. Treatment of Staphylococcal Infections in the Young Infant with Tetracycline and Novobiocin in Combination

M. I. ABBOTT and H. D. RILEY JR. *Antibiotic Medicine and Clinical Therapy* [Antibiot. Med.] 8, 23-28, Jan. [received March], 1961. 17 refs.

There is some evidence that certain antimicrobial agents have a more potent action when used in combination than when given singly. An opportunity to evaluate such combined therapy arose during a recent outbreak of staphylococcal infection in the newborn nursery of the Children's Memorial Hospital, Oklahoma City, Oklahoma. Altogether 25 infants aged between one day and 5 weeks with proved staphylococcal infection were treated with a solution containing tetracycline, 125 mg., novobiocin, 62.5 mg., and potassium metaphosphate, 100 mg. in each 5 ml. Dosage, based on the amount of tetracycline, ranged from 12 to 25 mg. per lb. (26.5 to 55 mg. per kg.) body weight daily. The causative strains of staphylococci, which were coagulase-positive, were mostly Phage Type 70 or 44A. Severe pyoderma was present in 20 infants, septicaemia in 3, and pneumonia in 2. All these cases responded satisfactorily to the treatment except one with pneumonia. In addition, one out of 2 infants with streptococcal omphalitis also treated failed to respond. There were no side-effects from the treatment. I. Ansell

493. Cardiac Failure in Infancy

C. M. McCUE and R. B. YOUNG. *Journal of Pediatrics* [J. Pediat.] 58, 330-341, March, 1961. 7 figs., 15 refs.

A survey is presented of 115 consecutive cases of cardiac failure in infants under 2 years of age admitted to the Medical College of Virginia Hospitals, Richmond, between January, 1953, and January, 1960. The diagnosis was established by the presence of tachycardia, dyspnoea, and enlarged heart and liver, with or without cyanosis and oedema. The causes of heart failure in infancy, including the various forms of congenital defect, are outlined, and the signs, treatment, and outlook discussed for each group. (Children with pneumonia or bronchiolitis were not included.) Electrocardiography and radiological investigations were performed, together with cardiac catheterization, angiography, or retrograde aortography if required.

The high mortality (64% in this series) emphasizes the gravity of the condition, but the survey suggests that an increasing number of patients can be saved by adequate investigation of the underlying condition and careful treatment. Digitalis therapy is valuable in all but late cases of myocardial failure or cases of fibroelastosis, and is particularly of value in coarctation of the aorta, in which the best results are obtained if digitalis can prevent failure until the optimum age for surgery, that is,

about 6 years. In patients with patent ductus arteriosus surgery is needed at any age if the heart failure cannot be controlled medically, but even in these cases digitalis is a useful adjunct to treatment. In this series digitalization was successful in cases of arrhythmia, including paroxysmal supraventricular tachycardia, and in cases of myocarditis. Cardiac failure aggravated by severe anaemia was treated by frequent small transfusions of packed erythrocytes, varying from 3 to 5 ml. per lb. (6.5 to 11 ml. per kg.) body weight depending on the haemoglobin level. E. H. Johnson

494. Further Experiences in the Treatment of Phenylketonuria

A. MONCRIEFF and R. H. WILKINSON. *British Medical Journal* [Brit. med. J.] 1, 763-767, March 18, 1961. 21 refs.

Since the report by Woolf *et al.* (*Arch. Dis. Childh.*, 1958, 33, 31; *Abstr. Wld Med.*, 1958, 24, 144) further experience has been gained at the Hospital for Sick Children, Great Ormond Street, London, in the treatment of phenylketonuria, and in the present paper this is discussed with special reference to diet. The authors report the follow-up results in a case previously described in which after treatment the patient is now a little taller and heavier than her non-affected twin sister. They note that even if the intelligence is not raised satisfactorily children receiving the low-phenylalanine diet become more manageable and fits or eczema cease. If treatment is started in the 2nd year of life the I.Q. score may rise by as much as 50%, but in some cases, even if the diet is strictly followed, it may fall again, while a marked fall may occur when the special diet is stopped. Good results may be obtained when the treatment is begun in early infancy, a routine test at 3 weeks of age being the optimum time for diagnosis, but if it is known that relatives of the infant suffer from phenylketonuria the test may be performed even earlier. False negative test results may arise if the urine is not fresh, unless a little chlorbutal or methiolate has been added to it, and "phenistix" must be dipped quickly in and out of the urine, since the reagents are leached out after a second or two. The various causes of false positive reactions were fully discussed by Gibbs and Woolf (*Brit. med. J.*, 1959, 2, 532; *Abstr. Wld Med.*, 1960, 27, 258).

In one patient, during tonsillitis with fever, phenylpyruvic acid reappeared in the urine and the blood phenylalanine level rose, but on recovery both values reverted to normal without change of diet. Cases are reported of patients who failed to gain weight on the special diet. It was found that the addition of milk to the diet corrected this fault, but the quantity needed varied with each patient. The importance of detecting heterozygote carriers of the affected gene is stressed and more exact methods are being investigated. Meanwhile it is noted that, by the present somewhat inaccurate methods, the parents (with certain exceptions) and some two-thirds of the patient's siblings show a lowered tolerance for phenylalanine.

[The number of cases which form the basis of this paper is not clearly stated.] G. de M. Rudolf

495. Results of Treatment in Phenylketonuria

S. COATES. *British Medical Journal* [Brit. med. J.] 1, 767-771, March 18, 1961. 14 refs.

At the Hospital for Sick Children, Great Ormond Street, London, in assessing the results of treatment in patients with phenylketonuria the Griffiths mental development scale was used for children with mental ages below 2 years and the Merrill-Palmer and the revised Stanford-Binet scales for those of higher grade. The tests were performed before starting the diet and repeated at 3, 6, and 12 months and thereafter yearly.

Of 29 male and female patients aged from 4 to 455 weeks (22 being aged over 52 weeks) who had been treated for 30 to 304 weeks, 22 showed a rise in their I.Q. ranging from 2 to 38 points. The mean weekly rate of improvement varied from 0.01 to 0.26 point; the quotient later decreased by 1 to 7 points in 6 cases. Of 3 patients treated for 112 to 221 weeks and followed up for 56 to 90 weeks after the end of treatment, there was a decrease in the I.Q. score in 2. Of the total number of patients, 5 showed psychoses. The mean rise of the quotient among these was 4 points, whereas in 7 non-psychotic cases with comparable initial quotients the I.Q. rose by 16 points.

The damage to the brain does not seem to affect locomotor development. No significant statistical evidence was obtained of factors influencing the effect of treatment.

[These children were apparently out-patients and reliance seems to have been placed on the statements of those in charge of them that the patients received the diet regularly.]

G. de M. Rudolf

496. Phenylketonuria: City of Birmingham Screening Survey

M. M. M. BOYD. *British Medical Journal* [Brit. med. J.] 1, 771-773, March 18, 1961. 10 refs.

In an effort to prevent the mental retardation associated with phenylketonuria arrangements were made in Birmingham to test all children born during 1959 and living in the city at the age of 6 weeks. Of 18,981 infants aged from 6 weeks to 3 months of age whose wet napkins were tested by health visitors (after instruction) with "phenistix" for about 30 seconds, 4 were reported to give a positive result. Further investigation by paper chromatography of a sample of urine showed that 3 of these infants were excreting less than 15 mg. of phenylpyruvic acid per 100 ml. Subsequently, 2 of the 3 gave normal results and developed normally; a second specimen of urine was not obtained from the third child. There was thus only one confirmed case, an incidence of 1 in 19,000, that is, approximately the expected mean rate.

G. de M. Rudolf

497. Control of Respiratory Infections in Children by Tetracycline

N. WYNN-WILLIAMS. *British Medical Journal* [Brit. med. J.] 1, 469-471, Feb. 18, 1961. 1 ref.

An investigation was carried out at the Bedford General Hospital to determine whether a therapeutic dosage of tetracycline for 2 days at the start of an upper respiratory infection would prevent the development of bronchitis

or disabling chest colds in young children. Included in the study were 96 children aged between 2 and 12 years who had a past history of frequent colds going on to the chest. These were divided at random into 2 equal groups, one group being given medicine containing tetracycline and the other a similar mixture with no tetracycline. The mother was told to give the child a course of 6 doses of the medicine at approximately 6-hourly intervals as soon as she suspected that an infection had begun.

During the autumn and winter of 1959-60 there were 210 infections among the children given tetracycline and 186 in the control group. Attacks of bronchitis were prevented in 122 (58%) of the infections in the tetracycline-treated group and in 91 (49%) of those among the controls. Details of the distribution of attacks according to the duration of fever, stay in bed, and days off school are presented. The difference was significant only in regard to days away from school, the average times away from school per attack being 1.93 days for the treated group as against 2.95 days for the controls.

G. Clayton

498. The Changing Picture of Pneumonia and Empyema in Infants and Children

M. M. RAVITCH and R. FEIN. *Journal of the American Medical Association* [J. Amer. med. Ass.] 175, 1039-1044, March 25, 1961. 1 fig., 7 refs.

This report reviews the changing picture of pneumonia and empyema in infants and children as seen in out-patients attending the Harriet Lane Home of the Johns Hopkins Hospital, Baltimore, over a period of 25 years from 1934 to 1959. During this time there were 10,632 cases of pneumonia and 214 cases of empyema. The hospitalization rate averaged 28%, but fell during the period from 49 to 18%. However, in infants (aged less than 2 years) the rate remained fairly constant and the most recent figures show that 72% of such infants were admitted to hospital.

The incidence of empyema among patients admitted to hospital with pneumonia fell from 10% in 1934 to 2% in 1955, but has risen again recently with the increased frequency of staphylococcal infections, reaching 14% in 1955-8. Bacteriologically, the incidence of empyema due to pneumococci, *Haemophilus influenzae*, and streptococci has fallen dramatically. On the other hand that of staphylococcal empyema has risen equally dramatically and this type now accounts for 92% of all cases (89% in infants). There has not been a case of empyema caused by *H. influenzae* since 1944, none due to streptococci since 1948, and only 5 cases of empyema due to pneumococci since 1947. During the period 1955-8 there were 35 cases due to staphylococci, almost all of them occurring in infants.

It is concluded that "the effect of widespread antibacterial therapy appears to have been to decrease the need for hospitalization of children with pneumonia and to eliminate almost entirely the incidence of empyema due to the pneumococcus, the streptococcus, and the *H. influenzae*. This has been accompanied by a sharp rise in the number of empyemas due to staphylococci, almost all in infants".

John Fry

Medical Genetics

499. **Genetic Studies on the Congenitally Hypothyroid**
J. V. NEEL, E. A. CARR, W. H. BEIERWALTES, and R. T. DAVIDSON. *Pediatrics [Pediatrics]* 27, 269-285, Feb., 1961. 41 refs.

The authors describe, from the University of Michigan Medical School, Ann Arbor, a survey of 54 index patients with congenital hypothyroidism and their families. The patients were all investigated by modern methods, including thyroidal uptake of ^{131}I and chromatographic partition of iodine-containing constituents in the serum. The following classification of types of congenital hypothyroidism was adopted: (1) no evidence of any thyroid tissue; (2A) one clearly defined biochemical deficiency in thyroid hormone synthesis; (2B) several such biochemical deficiencies present; (2C) the nature of the biochemical defect not determined; and (3) failure of thyroid hormone, once released, to affect body cells. There were 34 patients with Type-1 hypothyroidism and 7 with Type 2A, the latter being all of the type involving a defect in the organic binding of iodine. The remaining 13 patients all had hypothyroidism of Type 2C. The authors note, however, that this classification is not yet entirely satisfactory. Thus of 6 sibships containing 2 congenitally hypothyroid patients, there were 3 in which the elder child had the defect of Type 1 and the younger that of Type 2.

The sex ratio among Type-1 cretins was 8 males to 26 females, but in Type-2 cretins it was 16 males to 18 females. There was one marriage between second cousins among the parents of Type-1 cretins, but 2 first-cousin marriages among the parents of those of Type 2. Of the 30 siblings of Type-2A index patients, 12 were affected, whereas of the 28 siblings of Type-2C patients, only 2 were affected. Of 109 liveborn siblings of Type-1 patients, none were definitely affected. Studies of iodine uptake in the parents of Type-1 and Type-2 children revealed no abnormalities.

The authors conclude that in hypothyroidism of Type 2A recessive inheritance is implicated, and that this may also be the case for some patients of Type 2C. In regard to Type-1 cases, the authors tentatively put forward the view that they are casualties of genetic homeostatic mechanisms, having less than the proportion of heterozygous gene loci needed for orderly development.

C. O. Carter

500. **Heredity of Alzheimer's Disease.** (Zur Erblichkeit der Alzheimerschen Krankheit)
G. ZAWUSKI. *Archiv für Psychiatrie und Nervenkrankheiten [Arch. Psychiat. Nervenkr.]* 201, 123-132, 1960. 1 fig., 16 refs.

From the Psychiatric and Neurological Clinic of the University of the Saarland, Homburg, the author reports a family in which 9 established cases of Alzheimer's disease occurred over 3 generations. This finding is

considered to give support to the view that the disease is hereditary, but other possible interpretations are also discussed. The hereditary hypothesis is mainly supported by the great similarity of the clinical picture in all cases, leading to the reasonable conclusion that the pathological substrate is also of the same nature in all cases.

J. Hoenig

501. **Factors in the Causation of Persistent Ductus Arteriosus**

P. E. POLANI and M. CAMPBELL. *Annals of Human Genetics [Ann. hum. Genet.]* 24, 343-357, Dec., 1960. 49 refs.

We have made inquiries into the family history of 261 patients with persistent ductus arteriosus (P.D.A.) for evidence of genetic or environmental causes. Those with other malformations of the heart as well were excluded by definition: they would, however, have formed nearly one tenth of the total. Patients with P.D.A. have also a higher incidence than would be expected of non-cardiac malformations (6%). In the sibs of the propositi with P.D.A. congenital malformations of the heart were more common (2%) than would be expected by chance and generally the defect in a sib was homologous. In the parents and possibly in the children of the propositi, cardiac or other malformations were not specially common. Consanguinity of the parents was not very frequent (1.6% first cousins). Maternal age and birth order were not significant factors. The mean of the paternal ages was 3.3 years higher than that of the maternal ages: this is one year more than expected. More girls with P.D.A. were born in the second half of the year, especially from August to October. Boys followed the usual seasonal pattern of births. In general this agrees with the findings of Record and McKeown [*Brit. Heart J.*, 1953, 15, 376]. As usual, there were more females than males with P.D.A., the reason for this being obscure. The birth weights of our patients did not deviate greatly from normality.

Like Record and McKeown, we have frequently found a history of asphyxia and other difficulties at birth and during the neonatal period, but are disinclined to ascribe fully persistent patency of the duct to neonatal asphyxia.—[Authors' summary.]

502. **The Genetics of Pseudoxanthoma Elasticum**

G. M. BERLYNE, M. G. BULMER, and R. PLATT. *Quarterly Journal of Medicine [Quart. J. Med.]* 30, 201-212, April, 1961. 5 figs., 41 refs.

The mode of inheritance of pseudoxanthoma elasticum is considered by examining reports of a number of sibships each containing at least one person affected by the condition. Most of the reports have been published elsewhere, some are previously unpublished, and 3 are

described in detail with pedigrees for the first time. [Four further families, not used in the genetical analysis, are described in an addendum because they were investigated after the present paper was prepared.] The clinical features of the condition are described in detail, as are the clinical findings in the 7 families reported for the first time. The reports of 22 sibships were "complete" in that the total sibship size and sex composition is given and the parents were known to be unaffected. Six of these sibships included both males and females, but only males were affected. In a further 15 sibships, of which 10 had members of each sex, only females were affected. In the 6 sibships with affected males there were 9 affected males, 12 unaffected males, and 11 unaffected females. In the 15 sibships with affected females there were 21 unaffected males, 27 affected females, and 17 unaffected females. Only one sibship of the 22 completely reported had affected members of each sex; it was composed of one affected male and one affected female. Thus there were only 10 affected males and as many as 28 affected females in these 22 sibships; this female excess cannot easily be explained, although because of the skin condition concerned more frequent ascertainment of females could be expected.

A second group of 17 sibships which had at least 2 affected members was considered, but this group was "incomplete" in that no details of sibship size or sex distribution of unaffected members was reported. This group included 5 sibships each with 2 affected males and no affected females and 5 sibships each with no affected males and 2 affected females. In the 7 remaining sibships, in which at least one of each sex was affected, there were 10 affected males and 8 affected females. Thus in the incomplete series the number of each sex affected was similar, 20 males and 18 females.

The literature suggests that in most families the condition is transmitted by a recessive gene. Consanguinity of matings in families with affected members has been reported (3 instances are quoted) and the proportion of affected persons among the sibs of propositi ($16/77 = 0.21 \pm 0.05$) in completely reported families with unaffected parents is compatible with expectation on the hypothesis of transmission by a single recessive gene if single ascertainment of each family is assumed. There are only a few reports in which persons of different generations were affected (5 are mentioned). However, it is suggested that the inheritance in a few families could be due to partial sex linkage (a recessive gene located on the homologous portions of the sex chromosomes) and the authors examine very thoroughly this unlikely possibility. The main observation in favour of such a theory is that only in one of the 22 completely reported sibships were there affected persons of different sex. In contrast, however, is the observation that 7 of the 17 incompletely reported sibships were of this type. Although the families with affected members in 2 generations and those with consanguineous matings are individually considered, the authors, in summarizing their findings, cannot completely rule out occasional transmission by a partially sex-linked gene.

The main interest in the examination of relatives of affected individuals was to discover whether possible

heterozygotes had any detectable clinical features. In fact, abnormal visibility of choroidal vessels was found in unaffected members of 6 of the 7 families which the authors personally investigated, and in 2 instances this abnormality occurred in the families of both parents of the propositi. It is suggested that abnormal visibility of choroidal vessels is a condition shown by some heterozygote carriers of the recessive gene. E. A. Cheeseman

503. Multiple Osteomatoses, Fibromas, Lipomas and Fibrosarcomas of the Skin and Mesentery, Epidermoid Inclusion Cysts of the Skin, Leiomyomas and Multiple Intestinal Polyposis: a Heritable Disorder of Connective Tissue

R. J. GORLIN and A. P. CHAUDHRY. *New England Journal of Medicine* [New Engl. J. Med.] 263, 1151-1158, Dec. 8, 1960. 9 figs., 36 refs.

A syndrome which includes multiple osteomata, fibromata of the skin and mesentery, epidermoid inclusion cysts of the skin, and multiple intestinal polyposis is discussed, and the previous literature reviewed. Three families are described in which individuals showing this syndrome occurred. The familial distribution is consistent with the hypothesis that the affected individuals are heterozygous for rare abnormal genes.

H. Harris

504. The Single-X Nature of Sex Chromatin in Man

S. OHNO and S. MAKINO. *Lancet* [Lancet] 1, 78-79, Jan. 14, 1961. 2 figs., 11 refs.

Squash preparations of liver cells from a human foetus of each sex at about the 4th month of gestation were stained by the Feulgen method. Cells of the female foetus at prophase showed one densely stained chromosome which corresponded in size with the sex chromatin mass of cells at interphase and with a presumed X chromosome of cells at metaphase. In the male foetus a dense mass in interphase nuclei, smaller than the sex chromatin body, corresponded with a small dense chromosome at prophase and with the presumed Y chromosome of metaphase. These findings support the view that the sex-chromatin body seen in female interphase nuclei represents a single X chromosome.

G. C. R. Morris

505. Sex-chromatin Body in Normal Human Testis

J. S. S. STEWART and A. R. SANDERSON. *Lancet* [Lancet] 1, 79-80, Jan. 14, 1961. 2 figs., 2 refs.

Testicular tissue from 7 men aged 17 to 75 was obtained at biopsy or orchidectomy and examined in sections and squash preparations at Queen's College, Dundee. Nuclei in sections or oral mucosal smears were chromatin-negative in all cases; in 3 of them metaphase nuclei showed the normal chromosome number and XY sex constitution. But in all 7 sex chromatin was present in about 10% of germ-cell nuclei; it appeared in nuclei of different sizes, probably in spermatogonia and in primary and secondary spermatocytes.

This observation is taken to support the view that the sex-chromatin body is derived from the heterochromatic portion of a single X chromosome. G. C. R. Morris

Public Health and Industrial Medicine

506. Air-borne Staphylococci and the Control of Hospital Cross-infection

C. G. A. THOMAS and P. D. GRIFFITHS. *Guy's Hospital Reports [Guy's Hosp. Rep.]* 110, 76-86, 1961. 2 figs.

The incidence of *Staphylococcus aureus* in the air of the hospital was studied at Guy's and the Evelina Children's Hospitals, London, exposed nutrient agar plates being used. Over the whole period of the study some wards such as the obstetric unit had a low average count of *Staph. aureus*, while in other wards, particularly the two wards for skin patients, the counts were very high. The average count in the septic ward was surprisingly low and the average count in the 6 medical wards was higher than that in the most contaminated surgical ward. However, the counts of *Staph. aureus* in most wards varied greatly from week to week and no significance could be attached to minor differences in average counts.

There was no precise relationship between the number of infected cases in a ward and the counts of *Staph. aureus* in the air; the air might be grossly contaminated at a time when the percentage of infected cases in the ward was very low. Alternatively, a ward might pass through a period with a relatively high infection rate and yet the air remained remarkably clean. On days when the counts were high the staphylococci were more resistant to antibiotics than on days when the counts were low. Patients with superficial infections, such as skin disease and infected burns, were the chief disseminators of *Staph. aureus*. Septic surgical wounds were responsible for only 3 of the high counts in adult surgical wards and for none in the children's hospital. On three occasions in the adult surgical wards the high counts were recorded when there were no known cases of *Staph. aureus* infection in the ward.

The authors conclude that sampling the air of hospital wards is of only limited value in deciding which patients should be isolated, since most of these patients can be recognized on clinical grounds. Patients with skin diseases and infected burns are potentially very dangerous.

H. Caplan

507. *Brucella abortus* in Milk in England and Wales in 1959

A REPORT OF THE PUBLIC HEALTH LABORATORY SERVICE. *Monthly Bulletin of the Ministry of Health and the Public Health Laboratory Service [Monthly Bull. Minist. Hlth Lab. Serv.]* 20, 33-36, Feb., 1961. 2 refs.

The results of routine examinations carried out in 1959 by 35 public health laboratories throughout England and Wales for the presence in milk of brucellae and, incidentally, of tubercle bacilli are reported.

The milk tested was "herd milk" (that is, bulked milk from different herds was excluded) and it was usually examined by centrifuging 50 ml. of the milk, mixing the sediment with 1 ml. of its cream, and injecting the mixture

intramuscularly into the thigh of a guinea-pig. Six weeks later the animal was killed and examined for tuberculosis and at the same time cultures from the lymphatic nodes and spleen were made for brucellae.

Brucellae were demonstrated in 544 (4.8%) of 11,450 samples of milk examined. Of 390 strains typed, 93.6% were shown to be *Brucella abortus* and 6.4% *Br. melitensis*. It is emphasized that although these results are not the outcome of an investigation organized for this specific purpose, they do show that the prevalence of brucella infection varies in different parts of the country, being highest in the North-West and lowest in the South-West. It is thought that these results underestimate the true incidence, which is probably about 15%, and reasons are advanced for this belief.

A. E. Wright

508. Salmonellae in a Poultry-processing Plant

J. M. S. DIXON and F. E. POOLEY. *Monthly Bulletin of the Ministry of Health and the Public Health Laboratory Service [Monthly Bull. Minist. Hlth Lab. Serv.]* 20, 30-33, Feb., 1961. 6 refs.

From the Public Health Laboratory, Ipswich, comes this report of an investigation into the occurrence of salmonellae in and around a factory processing and packing 12,000 "broiler chickens" daily. Specimens for bacteriological examination were taken of the water in the tanks in which the carcasses were washed and chilled, from the carcasses themselves, from edible viscera (heart and liver), and from the hands of factory operatives and were incubated at 37° C. in a selenite-F broth and subcultured on to brilliant-green MacConkey agar and Wilson and Blair's medium.

It was found that of a total of 544 specimens (which had been collected weekly over a period of 23 weeks), 75 (13.8%) were positive for salmonellae. The commonest organism isolated was *Salmonella typhimurium*, but seven other types were detected. The authors consider that the maximum dissemination of the organisms occurred at the stage of evisceration, but that contamination of the water in the chilling tanks was also heavy. They conclude by pointing out that although the number of viable salmonellae on the final product—the frozen bird—must be very small, nevertheless "the introduction into kitchens of any foodstuff harbouring even small numbers of salmonellae is a potential hazard to health".

A. E. Wright

509. Mortality Studies in Relation to Air Pollution

J. RUMFORD. *American Journal of Public Health [Amer. J. publ. Hlth]* 51, 165-173, Feb., 1961. 5 figs.

The author describes some studies correlating death rates from various diseases and air pollution as measured by dustfall in different parts of the same city and also at different times in the same city. In Philadelphia correlations between mortality and four socio-economic indices

were also calculated. "Pneumonia and arteriosclerotic heart disease were apparently equally influenced by variation in dustfall and socioeconomic variables. Variation in mortality from chronic rheumatic heart disease was more strongly related to dustfall than to any of the indexes of socioeconomic condition which were used". In a study of white female mortality rates in Chicago the mortality rates were higher in manufacturing than in non-manufacturing areas. "The difference was greatest for cancer and tuberculosis of the respiratory tract, chronic rheumatic and hypertensive heart disease, and other diseases of the heart."

[A graph purporting to show a relationship between daily dust count, cardiovascular mortality, and temperature is unconvincing. The absence of adequate pollution data and of details of populations defined by age and sex prevent the drawing of any definite conclusions from this paper.]

John Pemberton

510. A Small-scale Field Trial with a Type 3 Attenuated Poliovirus in a Communal Settlement

S. LEVINE, N. GOLDBLUM, O. MOSCOVICI, and R. HORETZKY. *American Journal of Hygiene* [Amer. J. Hyg.] 73, 10-19, Jan. [received March], 1961. 6 figs., 18 refs.

This paper from the Ministry of Health Virus Laboratory, Tel Aviv-Yaffo, Israel, reports the results of a study of the infectivity of oral attenuated poliomyelitis vaccine, the duration of its excretion, and its spread. Interference by other enteroviruses and the effects of re-feeding were observed. The study was carried out in a semi-closed community with a population of 452, of whom 132 were children. Most members of the settlement were already protected by Salk vaccine. Type-3 Lederle attenuated virus in a dose of $10^{6.5}$ T.C.D.₅₀ was fed to 2 or 3 children in each household. Of the 23 children fed initially, 22 were re-fed 8 months later and a similar number were given a placebo.

Only 3 of 180 prefeeding sera did not have antibodies, and of 136 prefeeding stools, 11 (8%) contained enteroviruses other than poliomyelitis. After feeding, stools were collected daily for 10 days and bi-weekly thereafter for 6 weeks. In 2 to 3 days 22 of the children excreted virus, the younger group (0 to 2 years) doing so for 32 to 43 days, but the older group (2 to 13 years) for 6 to 10 days only (with 2 exceptions). Among the home contacts infection decreased with age; thus in the group 0 to 2 years 10 out of 14 (71%) became infected; 2 to 4 years, 4 out of 14 (28%) became infected; and 5 to 13 years, only 3 out of 67 (4.5%) became infected. Of 22 children infected primarily with Type-3 vaccine, 7 were reinfected on the second feeding.

A. E. Wright

511. Theory and Observation in Family Epidemic of the Common Cold

M. A. HEASMAN and D. D. REID. *British Journal of Preventive and Social Medicine* [Brit. J. prev. soc. Med.] 15, 12-16, Jan., 1961. 10 refs.

Details previously published (Brimblecombe *et al.*, *Brit. med. J.*, 1958, 1, 119; *Abstr. Wld Med.*, 1958, 24, 72) of a series of infections with the common cold in

664 families, each of 2 parents and 3 children, were analysed at the London School of Hygiene and Tropical Medicine to test the adequacy of the description of biological processes given by different epidemiological theories. Major Greenwood (*J. Hyg. (Camb.)*, 1931, 31, 336) introduced the idea that the spread of measles within a household could be described in terms of a chain of chance events which followed the usual binomial expression of the law of probability, and the authors present a table showing the observed and expected distribution of colds in completed family epidemics in which the fit is excellent. Greenwood's theory assumes a brief period of infectiousness followed by a relatively long and constant incubation period, but an even better fit is given by the theory of Reed and Frost (Bailey, "The Mathematical Theory of Epidemics", London, 1957) which postulates an increased risk of infection when more than one infectious case is circulating in the home, and a further improvement is obtained by applying it to groups of families living in similar degrees of domestic overcrowding. The same data might, however, be as well fitted by some alternative theory, and Bailey (*J. roy. statist. Soc., B*, 1955, 17, 35) has evolved a further model based on the mixing of continuously infective sources with a group of susceptibles among whom the incubation period varies, which fits particularly well to data from outbreaks in crowded homes.

The authors conclude that there is still a need for the development of alternative theories of the mechanics of epidemic behaviour.

F. T. H. Wood

512. Epidemiologic Observations on Two Outbreaks of Asian Influenza in a Children's Institution

J. A. BELL, J. E. CRAIGHEAD, R. G. JAMES, and D. WONG. *American Journal of Hygiene* [Amer. J. Hyg.] 73, 84-89, Jan. [received March], 1961. 1 fig., 5 refs.

Two outbreaks of Asian-type influenza occurring in a period of 6 months in a children's institution are described in this paper from the National Institute of Allergy and Infectious Diseases, Bethesda, Maryland. The institution is a relatively isolated community housing physically and mentally normal children, aged between 3 and 17 years, for social reasons, the children living in groups according to age. More than half the children at risk during the second outbreak had been admitted to the institution between the two epidemics, thus permitting a study to be made of the 6-month persistence of natural immunity to influenza and also a comparison of the outbreaks.

In the first outbreak one isolation of Asian influenza virus was made and high convalescent titres were found in 5 of 7 specimens of serum. In the second outbreak 3 isolations of Asian-type virus were obtained. The first epidemic spread slowly throughout the community over a period of 37 days, in contrast to the second, which was over in 12 days. In the first outbreak 153 (69%) of 223 children were attacked, while in the second 72 (28%) of 259 were affected. Only 12 (11%) of 107 children ill during the first epidemic were affected during the second, suggesting that a substantial degree of immunity had

persisted over 6 months. Of 42 children who did not have clinical influenza during the first outbreak, 7 (17%) were attacked in the second, suggesting that some children developed immunity to infection without any recognizable illness.

A. E. Wright

INDUSTRIAL MEDICINE

513. Allergy to Raw Coffee—an Occupational Disease
M. KAYE and S. O. FREEDMAN. *Canadian Medical Association Journal* [Canad. med. Ass. J.] 84, 469-471, March 4, 1961. 4 refs.

Employees at a coffee processing plant in Montreal complained of coryza, dermatitis, lacrimation, and bronchial spasm, which occurred separately or in combination and appeared to be caused by dust arising out of the processes. The raw green beans were delivered to the factory in bags, which were emptied manually into machines for separating the chaff from the beans; this process was very dusty. The subsequent operations were successively roasting, packing, and dispatching. Little or no adverse effect was observed among the men employed in packing and dispatching the beans.

As the symptoms suggested an allergic reaction an attempt was made to isolate the allergen. Intradermal injections of various dilutions of aqueous extracts of raw chaff, raw beans, roasted chaff, and roasted beans were given to three groups of employees: (1) 17 who had had no contact with coffee manufacturing in the plant, mostly office personnel; (2) 39 suspected of having allergic symptoms; and (3) 56 working in the plant and usually, but not always, having contact with the raw and prepared coffee but who had no symptoms. It was found that the allergic reactions were caused by the chaff of the raw coffee and occurred predominantly in subjects with a pre-employment history of allergic symptoms. Palliative measures included reducing the content of chaff dust in the air and excluding from employment workers with a previous history of asthma, hay-fever, or bronchitis. [It is some assurance that none of the allergic patients, with one possible exception, had any symptoms associated with drinking coffee.]

A. Meiklejohn

514. The Effect of a Diplococcal Antiserum in the Treatment of "Chinga". (Лечебное действие диплококковой сыворотки при чинге)
M. JA. ALFER'EVA and G. V. РОПОВ. *Клиническая Медицина* [Klin. Med. (Mosk.)] 42, 66-68, March, 1961. 12 refs.

During the first half of every year seals appear in the White and Barents Seas and a considerable sealing industry is set up. "Chinga" is a specific infectious disease that occurs among the workers in this industry, the organism responsible being a Gram-positive diplococcus, saprophytic in the organs of the seals. The incubation period is 2 to 30 days. The earliest symptom is pain, gradually increasing in severity, affecting the joints of the fingers, which begin to swell. The swelling lasts 1 to 2 weeks and there is no fever unless there is a secondary infection. There is very little lymphatic inflammation

and no change in the blood. There are 3 forms of chinga: para-articular, articular, and mixed. If untreated or treated only with local herbs the process results in ankylosis or contractures. Blocking with procaine and physiotherapy have some beneficial effect.

For the past 6 years the authors have been using a diplococcal antiserum, which was first tested on rabbits, and have treated 88 patients ranging in age from 17 to 60, mostly with the para-articular variety of chinga. The mean duration of treatment was 25 days. The function of the joints recovered completely in 85 cases, one patient developed ankylosis and 2 contractures. If treatment is started early the total amount of antiserum required is 4 to 8 ml., but larger amounts are necessary if treatment is started late.

H. W. Swann

"Seal finger" has been described (Hillenbrand, *Lancet*, 1953, 1, 680; *Abstr. Wld Med.*, 1954, 15, 89) as an occupational disease among sealers in the South Atlantic and Antarctic, but this appears to be a more superficial condition than chinga, resembling cellulitis or erysipelas. It would be interesting to know, however, whether a similar organism is involved in the two diseases.—EDITOR.]

515. The Action of Carbon Disulphide on Cerebral Monoamine Oxidase

M. MAGISTRETTI and E. PEIRONE. *Medicina del lavoro* [Med. d. Lavoro] 52, 1-10, Jan. [received April], 1961. 4 figs., bibliography.

Serotonin or 5-hydroxytryptamine (5-HT), a derivative of alimentary tryptophan, plays an important part in the physiology of the central nervous system; its breakdown is initiated by monoamine oxidase (MAO). If reserpine is given 5-HT is liberated in the cerebral substance and this is broken down by the action of MAO. Accumulation of large quantities of 5-HT in the brain may cause excitation, although a varied and often contradictory clinical picture is produced according to the site and the concentration of this amine in the central nervous system.

The authors of this paper from the University of Milan, having observed a similarity between the effects of carbon disulphide poisoning and those of known MAO inhibitors, studied the rate of disappearance of 5-HT from the brains of rats after the addition of varying concentrations of carbon disulphide. In experiments *in vitro* a solution of carbon disulphide was incubated with a brain-5-HT mixture, while in experiments *in vivo* rats were exposed to carbon disulphide vapour and killed at varying intervals thereafter. The results of both series of experiments clearly showed that the concentration of 5-HT rose in the carbon disulphide preparations, indicating MAO inhibition. In live rats there was no MAO inhibition after 72 hours. With small exposures little effect was noted, but if these were repeated within the recovery time MAO was progressively inactivated.

It is suggested that the observed influence of carbon disulphide on 5-HT metabolism might explain some of the neuropsychiatric features of carbon disulphide poisoning. Man has a higher tolerance to carbon disulphide than the rat.

Gavin Thurston

Toxicology

516. Delayed and Long-lasting Electrocardiographic Changes in Carbon-monoxide Poisoning

G. D. MIDDLETON, D. W. ASHBY, and F. CLARK. *Lancet* [Lancet] 1, 12-14, Jan. 7, 1961. 2 figs., 13 refs.

The authors, writing from the Gateshead Group of Hospitals, describe long-lasting electrocardiographic (ECG) changes in 2 survivors of carbon monoxide poisoning. In one case the carboxyhaemoglobin content of the venous blood was 23% on admission, but no estimation was made in the second case. Both patients had a high pulse rate. Serial ECGs are presented, and these show anoxic changes with depression of the RST segment in both cases.

In a survey of the literature on the subject the authors point out that, while little has been written about the heart in carbon monoxide poisoning, such information as there is indicates that the proportion of ECG changes is high. In the present cases the ECG took 70 to 100 days to return to normal, and this suggests that the myocardium may be more severely injured than has hitherto been thought. The authors refer to the finding of anoxic T-wave changes in mountaineers at over 16,000 feet (5,000 metres) and suggest that in future investigations estimations of serum transaminase levels to reveal myocardial damage would be of interest.

One of the patients, who was thyrotoxic, had conduction as well as myocardial ECG changes, and this would seem to confirm the impression that some individuals are more sensitive to carbon monoxide than others. The authors advise that, as the ECG picture may deteriorate after an initial improvement in cases of carbon monoxide poisoning, follow-up should be continued for some time.

Gavin Thurston

517. Delayed Cardiac Effects of Carbon Monoxide Poisoning. (Les accidents cardiaques retardés de l'oxyde de carbone)

Y. BOUVRAIN, M. GAULTIER, P. GERVAIS, and P. PASQUIER. *Semaine des hôpitaux de Paris* [Sem. Hôp. Paris] 36, 3163-3172, Dec. 12, 1960. 7 figs., 35 refs.

The authors state that some 2,000 cases of carbon monoxide poisoning occur in the Paris region every year and that of these about 5% are admitted to hospital in coma. After an extensive review of previously described cases they present 2 more, with special reference to delayed cardiac effects. Both victims were admitted to hospital in a state of coma and showed sinus rhythm with an inverted T wave. The first patient, a man aged 52, had an extensor plantar reflex on both sides and lost the power of speech for some weeks. The abnormal electrocardiogram returned to normal on the 5th day, but the abnormalities reappeared on the 12th day and persisted for over 2 months. The second patient, a woman aged 36, showed no neurological symptoms other than the original coma and later mental confusion, but

suffered much precordial pain. It is suggested that the early symptoms are associated with a severe anoxaemia and those which return later with injury to the myocardium, with subendocardial haemorrhages and in some cases myocardial infarction. It is recommended that these patients should have prolonged rest and frequent supervision. The electrocardiographic findings in these 2 cases are described in detail and illustrated.

V. J. Woolley

518. Comparative Toxicology of Iron Compounds

L. C. WEAVER, R. W. GARDIER, V. B. ROBINSON, and C. A. BUNDE. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] 241, 296-302, March, 1961. 7 refs.

The large number of different iron preparations used in the treatment of iron-deficiency anaemia would seem to suggest that no one of them is universally acceptable. In this study the toxicity of 6 commonly used iron compounds was compared in mice, rats, and dogs with that of a new carbohydrate-iron complex having a molecular weight of about 30,000 and known commercially as "jeffron". When given by mouth, its LD₅₀ in mice was over 8,000 mg. per kg. body weight as compared with 1,025 mg. for ferrous sulphate and 3,950 mg. for ferrous gluconate. Intravenously it was slightly more toxic than iron-polysaccharide complex, but less so by the intraperitoneal route. The results in rats and dogs were similar. When given by mouth it caused no symptoms of gastric irritation, and no pathological lesions were found on histological examination post mortem.

V. J. Woolley

519. Treatment of Lead Poisoning with Intramuscular Edathamil Calcium-disodium

H. SHRAND. *Lancet* [Lancet] 1, 310-312, Feb. 11, 1961. 23 refs.

The diagnosis of lead poisoning is established when the blood level of lead exceeds 50 µg. per 100 g. of blood or the 24-hour urinary excretion of lead is above 80 µg. per litre. In the treatment of this condition "edathamil calcium-disodium" (sodium calciumedetate) is much less effective when given by mouth than when given parenterally and that intravenous administration involves the injection of large volumes of fluid, which may cause cerebral oedema.

The author of this paper from St. Mary's Hospital, London, describes 2 cases in which edathamil was given by intramuscular injection in a 5% solution with 0.5% procaine and 0.5% chlorocresol. The first patient, a boy aged 16 months, received 35 mg. per kg. body weight daily for 5 days and the second, a boy aged 2 years, received 75 mg. per kg. daily for a similar period. In the former patient the urinary excretion of lead rose to 430 µg. per litre after the 5 days. There was no local pain or reaction at the site of injection and both patients recovered completely.

V. J. Woolley

Anaesthetics

520. The Electroencephalographic Effect of Arrested Circulation in the Normothermic Human and Dog

V. L. BRECHNER, R. O. BAUER, R. W. M. BETHUNE, R. E. PHILLIPS, E. M. KAVAN, and J. B. DILLON. *Anesthesia and Analgesia; Current Researches* [Anesth. Analg. curr. Res.] 40, 1-14, Jan.-Feb., 1961. 8 figs., 18 refs.

Electroencephalographic response of dogs to circulatory standstill is presented. It is found that duration of a single circulatory arrest is correlated with duration of time lapse until onset of continuous electrical activity following restoration of circulation as a straight line when plotted logarithmically. A similar regression line has been described previously for the hypothermic human. The difference of the slope of these two lines indicates that the human electroencephalographic response, even during hypothermia, is more susceptible to ischemic trauma than the normothermic dog.

The records of 6 normothermic humans experiencing unexpected circulatory arrest are reviewed and prognostic criteria presented. A good prognosis is indicated by a return of continuous electrocortical activity within 15 minutes and a rapid progression of the activity to light levels of cerebral depression (fast frequency, low voltage) within 25 minutes of cardiorespiratory resuscitation.

Poor prognosis was indicated by a delay of more than 15 minutes in return of continuous electrocortical activity and little or no tendency for patterns, once established, to rapidly progress to levels of light cerebral depression. —[Authors' summary.]

521. Intravenous Barbiturate Anesthesia for Dental Outpatients

G. R. CHRISTENSON, C. L. HEBERT, and E. J. DRISCOLL. *Anesthesia and Analgesia; Current Researches* [Anesth. Analg. curr. Res.] 40, 77-86, Jan.-Feb., 1961. 4 figs., 5 refs.

The value of intravenous barbiturate anesthesia in dental surgery was studied at the National Institutes of Health, Bethesda, Maryland, in healthy adults undergoing dental extractions in a dental chair, the average duration of surgery being 18 to 20 minutes. Three agents were used: thiopentone (76 patients, 208 operations); methitural (24 patients, 82 operations); methohexitone (36 patients, 127 operations). Nervous patients were premedicated with quinalbarbitone ("secobarbital") by mouth and patients who required excessive amounts of the intravenously-administered barbiturate during the first operation received pethidine and/or nitrous oxide for second and subsequent operations. [These additional medications detract from the value of the results.]

In most patients there was a rise in blood pressure during anaesthesia and surgery with all three drugs. Complications encountered during anaesthesia included laryngeal spasm and copious salivation. The total doses of the drugs required for anaesthesia lasting 18 to 20

minutes were 516 mg. of thiopentone, 1,027 mg. of methitural, and 262 mg. of methohexitone. The postoperative course of the patients in the three groups is described; recovery was found to be most rapid after methohexitone.

Mark Swerdlow

522. Comparative Evaluation of Fluothane and Cyclopropane Anesthesia during Hemorrhagic Hypovolemia: Changing Concepts in the Management of Anesthesia (a Preliminary Report of Laboratory and Clinical Studies)

D. P. SMITH, L. W. FABIAN, and M. A. CARNES. *Anesthesia and Analgesia; Current Researches* [Anesth. Analg. curr. Res.] 40, 137-147, Jan.-Feb., 1961. 6 figs., 7 refs.

A comparative study of "fluothane" (halothane) and cyclopropane anaesthesia in haemorrhagic hypovolaemia is reported in this paper from the University of Mississippi Medical Center, Jackson. Unpremedicated mongrel dogs were first anaesthetized with 2% thiamylal and then a catheter was introduced into the inferior vena cava, monitoring instruments being attached to the animals. The dogs were allowed to awaken completely and were then anaesthetized again with either cyclopropane or halothane. The maintenance concentrations of the two anaesthetics were 12 to 16% and 0.8 to 1.6% respectively. Blood was withdrawn from the animals in fixed amounts and at fixed intervals so that the blood volume was reduced to 50% in 45 minutes. After an interval of 15 minutes re-infusion of blood was begun and was completed by stages in 45 minutes. The experiments were repeated later (on those animals which survived the original experiment), the cyclopropane group receiving halothane and those which had been given halothane receiving cyclopropane. The results indicated that tolerance to severe haemorrhage was greater during halothane than during cyclopropane anaesthesia.

The authors also studied the response of hypovolaemic patients to anaesthesia with cyclopropane (8 patients) and halothane (12 patients). The results were inconclusive, but suggested that the patients anaesthetized with halothane tolerated hypovolaemia better than those receiving cyclopropane.

Mark Swerdlow

523. Acid-Base Changes under Halothane, Nitrous Oxide and Oxygen Anaesthesia during Spontaneous Respiration. [In English]

M. H. HOLMDAHL and J. P. PAYNE. *Acta anaesthesiologica Scandinavica* [Acta anaesth. scand.] 4, 173-180, 1960 [received Feb., 1961]. 14 refs.

The effects of 1.5% halothane on respiration in patients undergoing surgery were studied by means of assessing the acid-base status of arterial blood. The depression of spontaneous respiration and rise in carbon dioxide tension were found to be less than earlier reported during halothane anaesthesia without concomitant surgery. Earlier findings that halothane does not cause metabolic

acidosis in patients under controlled respiration were confirmed in patients allowed to breathe spontaneously. The effect of halothane on the metabolic rate is discussed. —[Authors' summary.]

524. The Effect of Halothane on the Newborn Infant Delivered by Caesarean Section

J. B. MONTGOMERY. *British Journal of Anaesthesia* [Brit. J. Anaesth.] 33, 156-160, March, 1961. 1 fig., 10 refs.

A comparison has been made of the results following the use of two techniques of anaesthesia for Caesarean section. Thiopentone, suxamethonium, nitrous oxide and oxygen (artificial ventilation) caused less foetal depression than thiopentone, suxamethonium, nitrous oxide and oxygen with halothane (spontaneous respiration). —[Author's summary.]

525. Oxygen Utilization by Dogs after Administration of Potassium Perchlorate, during Hypothermia, and at a Pressure of 2 Atmospheres

R. TANAKA, M. FUJIMORI, and R. W. VIRTUE. *Anesthesiology* [Anesthesiology] 22, 20-23, Jan.-Feb., 1961. 6 refs.

Oxygen consumption diminishes consistently with decreasing body temperature, with reduced thyroid activity, and with administration of potassium perchlorate. Some workers have attempted to make internal oxygen supply last for a prolonged period of circulatory occlusion by carrying out surgical procedures within a tank at 3 atmospheres pressure of oxygen. [No mention is made of the possibility of oxygen poisoning, well known to divers, being produced at this pressure.] In an investigation at the University of Colorado Medical Center, Denver, these methods and different combinations of anaesthetic drugs and relaxants were tested in dogs. It was found that administration of potassium perchlorate and exposure to oxygen at high pressure had little effect and conferred little benefit. The use of such methods is not, therefore, considered justifiable.

W. Stanley Sykes

526. The Respiratory Effects of Resistance to Breathing in Anesthetized Man

J. F. NUNN and T. I. EZI-ASHI. *Anesthesiology* [Anesthesiology] 22, 174-185, March-April, 1961. 10 figs., 13 refs.

The respiratory effects of resistance to breathing have been studied in 28 patients anesthetized for routine surgery but permitted to breathe spontaneously. Resistances were imposed for periods of 2 to 7 minutes and ventilation was then compared with the control periods of unobstructed breathing.

The passage of inspired and/or expired gas through a water trap (threshold resistor) produced less than the expected reduction in ventilation since there was an immediate, presumably reflex, augmentation of the developed inspiratory tension. Thereafter there was a further increase in ventilation probably due to CO₂ retention—full compensation being achieved in 2 to 3 minutes. There was a wide scatter in the ability of patients to com-

pensate. Some patients attained a minute volume close to the control value against as much as 17 cm. water, while the worst response was apnoea at 12 cm. water with proportionate reduction against lower pressures.

A second study was concerned with flow-dependent resistors—two short, narrow tubes which offered the same resistance as 24 F and 16 F endotracheal tubes respectively. The reduction in ventilation was in accord with the results obtained on threshold resistors and amounted to a mean reduction of 7% with the 24 F resistor, and 21% with the 16 F resistor.

Finally a study was made of the effect of external pressure on the sternum or epigastrium. Weights up to 20 kg. on the sternum reduced the functional residual capacity but had no significant effect upon the ventilation. On the other hand 5 kg. on the epigastrium caused a mean reduction of ventilation of 18%.

It would appear that reflex compensation for resistance to breathing is well marked during anesthesia and in its absence the effects would be much more pronounced. In the present study, the ability to compensate was not found to be impaired by halothane, small doses of relaxants, old age or early emphysema. —[Authors' summary.]

527. Axillary Block of the Brachial Plexus

R. H. DE JONG. *Anesthesiology* [Anesthesiology] 22, 215-225, March-April, 1961. 5 figs., 13 refs.

Between April, 1959, and October, 1960, brachial plexus block was carried out by the axillary approach on 94 occasions in 93 patients at the United States Army Hospital, Munich, with complete success in 86 (91.5%). This route was chosen because of the high incidence of pneumothorax following the supraclavicular approach. From observations of 7 complete anatomical dissections of the axilla performed on fresh cadavers of adults and premature infants the author describes the anatomy of the brachial plexus in the axilla in detail. His technique of operation is as follows. The patient is positioned with the upper arm at a right angle to the body and the forearm flexed with the dorsum of the hand resting on the table, so that the brachial plexus is stretched and fixed. The axillary artery is palpated and the most proximal point in the axilla where it can be felt easily is chosen as the site of injection. After raising a skin wheal some solution is injected into the subcutaneous tissues to block the intercostobrachial nerve and the medial cutaneous nerve of the arm. A 26-gauge, $\frac{1}{4}$ -inch (12.6-mm.) needle is then advanced towards the artery and through the axillary fascia, which gives a characteristic feeling of resistance as it is penetrated. The signs of entry of the needle point into the neurovascular compartment are parasthesiae down the arm or the aspiration of blood into the syringe. Local anaesthetic solution (1% lignocaine with 1 in 250,000 adrenaline) is injected both anterior and posterior to the artery, the amount given being calculated to fill the neurovascular compartment. In an adult male this is 42 ml.; less is required for women, children, and debilitated patients. Complete block of all the nerves usually occurs in 15 minutes and the analgesia lasts for 3 hours. The only complication encoun-

tered was hyperaesthesia of the ulnar nerve in one case which lasted 24 hours. The author claims that this axillary block is more acceptable than other approaches to the plexus because of the ease and safety of performance and the absence of major complications.

J. V. I. Young

528. A Comparison of Supraclavicular and Axillary Techniques for Brachial Plexus Blocks

L. BRAND and E. M. PAPPER. *Anesthesiology* [Anesthesiology] 22, 226-229, March-April, 1961. 6 refs.

The results obtained from 230 supraclavicular blocks were compared with those obtained from 246 axillary brachial blocks. The axillary blocks resulted in a higher rate of success (91.5% versus 84.4%) and a lower incidence of complications (2.0% versus 7.1%). The serious complication of pneumothorax was completely eliminated.—[Authors' summary.]

529. The Inflated Stomach as an Accidental Phenomenon in Anaesthesia for Angiocardiography. [In English]

E. CARLSSON and A. WÄHLIN. *Acta anaesthesiologica Scandinavica* [Acta anaesth. scand.] 5, 39-46, 1961. 2 figs., 12 refs.

The effect of experimental inflation of the stomach has been studied in dogs. The object was to assess the possibility of reflex disturbances by accidental inflation of the stomach during anaesthesia in angiocardiography, using positive-pressure artificial ventilation with a mask and breathing bag, as an alternative to intubation. It is found that inflation of the stomach has only a strikingly small effect on the pressure conditions in the large thoracic vessels. The effect on the large vessels in the abdominal cavity is more pronounced. The only changes in the ECG [electrocardiogram] observed were those caused by the influence of the elevated diaphragm on the electric axis of the heart.—[Authors' summary.]

530. Hiatus Hernia: an Anaesthetic Hazard

O. P. DINNICK. *Lancet* [Lancet] 1, 470-473, March 4, 1961. 3 figs., 29 refs.

The author of this paper from the Middlesex Hospital, London, sets out to show that the high incidence of hiatus hernia in pregnant women may partly explain why regurgitation is a common hazard of obstetric anaesthesia and reports 13 cases of regurgitation during anaesthesia in which the diagnosis of hiatus hernia was based on clinical or radiological evidence. He states that unexpected regurgitation occurs in about one in 500 cases, but the incidence in obstetric anaesthesia is 2%. All patients who regurgitated were fat and the difficulties of anaesthetizing obese patients are noted. The conditions which must obtain for regurgitation to take place include the presence of fluid in the stomach, an incompetent cardia, a higher pressure in the stomach than in the oesophagus, and relaxation of the cricopharyngeus. Forceful, obstructed inspiration could be the determining factor in a patient with a tendency to regurgitate.

It is suggested that the anaesthetist should be on the look-out for symptoms of hiatus hernia—heartburn, retrosternal pain, or postural oesophageal reflux—

especially if the patients are fat, over 50 years of age, or in late pregnancy. If a positive history is obtained anaesthesia should be induced by one of the techniques used in cases of intestinal obstruction, the most suitable method probably being introduction of an endotracheal cuffed tube as soon as possible after anaesthesia has been induced in the reverse Trendelenburg position.

J. V. I. Young

531. Promethazine: Its Influence on the Course of Thiopentone and Methohexital Anaesthesia

J. MOORE and J. W. DUNDEE. *Anaesthesia* [Anaesthesia] 16, 71-73, Jan., 1961. 30 refs.

An investigation of the influence of promethazine on the course of anaesthesia with thiopentone and methohexital was carried out on patients undergoing uterine curettage with or without dilatation of the cervix at Musgrave Park Hospital, Belfast. Premedication was with (1) atropine, 0.6 mg.; (2) promethazine, 50 mg., and atropine, 0.6 mg.; (3) pethidine, 100 mg., and atropine, 0.6 mg.; or (4) pethidine, 100 mg., promethazine, 50 mg., and atropine, 0.6 mg. These drugs were administered 45 to 75 minutes before operation in random order, using the double-blind technique. Anaesthesia was induced with thiopentone, 4 mg. per kg., or methohexital, 1.6 mg. per kg., and maintained with nitrous oxide and oxygen (6:2) in semi-open circuit. Further doses of the barbiturates were given if necessary to control movements.

Promethazine was found to increase the incidence of excitatory phenomena with methohexital, but not with thiopentone; there was no effect on the incidence of coughing, hiccup, or laryngeal spasm with either anaesthetic. The use of promethazine produced a significant increase in the total requirement of both methohexital and thiopentone; the results also suggested that it caused an increased incidence of hypotension and exerted an anti-emetic effect. The authors conclude that the use of promethazine for premedication is inadvisable, particularly before methohexital anaesthesia.

Mark Swerdlow

532. Phenazocine: a New Synthetic Narcotic for Pediatric Premedication

J. A. YOUNG, R. B. N. BROWN, and R. M. SMITH JR. *Anesthesia and Analgesia; Current Researches* [Anesth. Analg. curr. Res.] 40, 213-219, March-April, 1961. 1 fig., 2 refs.

This investigation of the recently (1959) synthesized narcotic phenazocine was carried out at Allentown Hospital, Allentown, Pennsylvania, on 318 paediatric patients over 6 months of age undergoing a variety of surgical operations (principally tonsillectomy) who were premedicated with phenazocine and scopolamine administered intramuscularly one hour before operation. The dosage of phenazocine was 0.015 to 0.02 mg. per lb. (0.033 to 0.044 mg. per kg.) body weight. The pre-operative state and behaviour of the patients during induction and maintenance of anaesthesia were recorded. A variety of anaesthetic techniques were employed.

The authors found that, over-all, phenazocine gave adequate sedation in 80% of cases, sedation being opti-

mum in 54% and moderate in 26%; for various reasons it was slight or inadequate in 20%. They also found that it was easier to maintain a light plane of anaesthesia with phenazocine than with other narcotics used as supplements. The induction of anaesthesia was considered to be "smooth" in 71% of cases, while maintenance was smooth and untroubled in 76%. The chief complication was respiratory depression, the incidence of which varied directly with depth of anaesthesia. The authors note that with phenazocine as premedication patients may slide rapidly from the middle of Plane II into Plane IV, Plane III being difficult to maintain. However, owing to the excellent analgesic properties of phenazocine, surgery can be performed with a lighter plane of anaesthesia, which has the additional advantage that emergence is rapid and recovery time may be shortened by as much as 50%.
Mark Swerdlow

533. A New Intravenous Anaesthetic—G29505

M. SWERDLOW. *British Journal of Anaesthesia* [Brit. J. Anaesth.] 33, 104–108, Feb., 1961. 2 figs., 6 refs.

G29505 is a useful anaesthetic agent for operations or procedures of very brief duration. Supplemented by a mixture of nitrous oxide and oxygen it provides satisfactory anaesthesia for more prolonged superficial operations. It may also have distinct advantages as an induction agent before other forms of anaesthesia and its use for this purpose in obstetric anaesthesia particularly must be investigated. The use of G29505 by repeated injections does not appear to be advantageous. The risk of venous irritation has been considerably reduced in the present preparation but efforts must be made to remove entirely the irritant effect of the drug. In the field of dentistry, for multiple extractions in both adults and children, the induction of anaesthesia with G29505 and supplementation with nitrous oxide and oxygen mixtures offers distinct advantages in pleasantness for the patient, ease of management of anaesthesia, speed of recovery and relative freedom from postoperative complications. For 1 to 4 simple extractions in adults a single dose of G29505 suffices. For the removal of a few teeth in children, however, the author's preferred method remains to ask the child whether he would prefer "something to smell" or a "prick in the hand".—[Author's conclusions.]

534. The Placental Transmission of Succinylcholine

F. MOYA and N. KVISELGAARD. *Anesthesiology* [Anesthesiology] 22, 1–6, Jan.–Feb., 1961. 1 fig., 41 refs.

Reported evidence of the placental transmission of succinylcholine (suxamethonium) has been contradictory. The authors of this paper from the Presbyterian Hospital and the Sloane Hospital for Women, New York, studied the concentrations of suxamethonium in maternal venous and umbilical cord blood following administration of clinical doses of the drug to 22 patients. It was found that when the drug was given to the mother in the usual clinical doses it did not appear in the umbilical vein blood. It is suggested that this barrier action may be due to enzymes, such as cholinesterase, or to a physical impediment such as lipid insolubility in the syncytium.

There is also the possibility that suxamethonium may cross the placenta and be rapidly destroyed in the infant. The authors consider that the most likely explanation is the low fat solubility of the drug and that conditions may exist which tend to weaken the barrier.

W. Stanley Sykes

535. Muscle Pains after Suxamethonium Chloride in Children

G. H. BUSH and F. ROTH. *British Journal of Anaesthesia* [Brit. J. Anaesth.] 33, 151–155, March, 1961. 4 figs., 9 refs.

An investigation was carried out [at Alder Hey Children's Hospital, Liverpool], to determine the incidence of muscle pains following the use of suxamethonium intravenously in children from 5 to 14 years old. The overall incidence was 10%, although in the group between 5 and 9 years old the incidence was only 3%. There was a significant difference in incidence between boys and girls. No correlation between the incidence of muscle fasciculations and postoperative pains could be found.

Possible reasons for the different incidence of muscle pains in children and adults are discussed. It is suggested that there are no valid objections on these grounds to the use of suxamethonium in children of the younger age group.—[Authors' summary.]

536. A Report on Mortality and Morbidity following 9,107 Hypotensive Anaesthetics

G. E. H. ENDERBY. *British Journal of Anaesthesia* [Brit. J. Anaesth.] 33, 109–113, Feb., 1961. 1 ref.

This series represents 10 years' work by the staff of the Queen Victoria Hospital, East Grinstead (a total of 5,407 cases), together with a further 3,700 cases anaesthetized by the author in other hospitals and clinics.

Nine fatalities occurred in association with the 9,107 hypotensive anaesthetics. Four of these, and possibly a fifth, were caused by inadequate ventilation. Air embolism, adrenal insufficiency and diabetic hypoglycaemia caused the other fatalities. In one patient cerebral complications were possibly the result of the hypotension. During the same period there was a total of 30,950 operations at Queen Victoria Hospital, East Grinstead, and these showed an over-all mortality of 20. No direct comparison is made between these figures and the hypotensive series because of the differing circumstances of death which they include, but it is significant to note that inadequate ventilation as the cause of death did not figure prominently, except in association with ganglion-blocking drugs and hypotension.

Cerebral thrombosis occurred in one patient. There were no other cerebral or mental complications. Cardiac massage successfully resuscitated one patient. Another patient collapsed at the start of operation but recovered before cardiac massage was commenced. No significant difference was noted in the vomiting rate when compared with a similar series of non-hypotensive anaesthetics. No other complications were reported which were attributable to the hypotension.—[Author's summary.]

Radiology

537. **Increases in the Cell Content of the Cerebrospinal Fluid during Air Encephalography.** (Zellzahlveränderungen bei fraktionierter Liquorentnahme während der Pneumencephalographie)

H. ROSKAMP. *Archiv für Psychiatrie und Nervenkrankheiten* [Arch. Psychiat. Nervenkr.] 201, 426-437, 1961. 2 figs., 7 refs.

At the Neurological Clinic of the University of Tübingen cerebrospinal fluid obtained during performance of air encephalography in 82 cases was examined for cell content under controlled conditions. Pleocytosis was uncommon and was found in only 13% of cases; there was no correlation with age, with the amount of fluid withdrawn, or with the amount of air replaced. In patients without organic brain lesions or in patients with conditions such as arteriosclerosis and senile degeneration in which no definite inflammatory changes occur air encephalography never produced pleocytosis. Pleocytosis due to air encephalography would therefore suggest the presence of organic brain disease, particularly an inflammatory process.

J. Hoenig

538. **Successful Radiographic Demonstration of the Human Circle of Willis**

R. A. KUHN. *Journal of the American Medical Association* [J. Amer. med. Ass.] 175, 769-772, March 4, 1961. 2 figs., 11 refs.

The author describes a technique for the demonstration of the circle of Willis in the living subject in which opacification of the vessels is achieved by means of retrograde injection of contrast material through a cannula in the right brachial artery. With sterile precautions and under local anaesthesia the right brachial artery is exposed through a 1-inch (2.5-cm.) incision high in the arm. Rapid retrograde injection of 50% "hypaque" (sodium diatrizoate) opacifies the brachial, subclavian, and innominate arteries as far proximally as the arch of the aorta. Arterial pressure in these trunks equilibrates with the injected volume of fluid within a fraction of a second, after which the direction of flow is reversed, the opaque medium escapes out of the branches of the innominate artery under the normal pressure existing for the individual being examined, and ascends the right carotid and vertebral arteries. The sharp surge of pressure produced by direct injection of the medium into the carotid, vertebral, or subclavian artery, as in previous methods, is thus avoided. An automatic film-changing device capable of allowing radiographs to be taken at high speeds is necessary to exploit the method fully. The left common carotid artery is compressed and films exposed in the occipital, lateral, and submentovertical projections.

The results confirmed previous suspicions, based on anatomical studies, that communication between the anterior part and the posterior part of the circle of Willis through the posterior communicating arteries is limited,

and remains so even under abnormal conditions in which adequate communication would be highly desirable in helping to reduce, for example, the damage from focal cerebral ischaemia or cerebral infarct. It is noteworthy that despite heavy concentrations of opaque medium in the right anterior and posterior segments of the circle, the posterior communicating artery was rarely seen and then only as a very feeble, slender filament. The author states that this method has now been used to demonstrate the cerebral circulation in over 300 adults and children without mishap.

J. MacD. Holmes

539. **Shoulder Arthrography**

R. L. SAMILSON, R. L. RAPHAEL, L. POST, C. NOONAN, E. SIRIS, and F. L. RANEY JR. *Journal of the American Medical Association* [J. Amer. med. Ass.] 175, 773-778, March 4, 1961. 9 figs., 8 refs.

This report from the University of California, San Francisco, confirms the value of contrast arthrography of the shoulder as a means of confirming the accuracy of a clinical diagnosis of soft-tissue lesions around the joint which had been established by previous workers and adds certain further observations. In addition to showing a high correlation with the clinical findings, the pre-operative radiological diagnosis in a series of 125 arthrograms was proved correct in the 30 shoulders subjected to operation. The technique as described may be performed on an out-patient basis with full aseptic precautions, using sodium diatrizoate as a contrast medium. The procedure is likely to be accompanied by mild discomfort following the injection, with soreness of the shoulder on the following day. In this series no infections of the joint occurred.

In a normal arthrogram the subscapularis bursa, with its prolongation beneath the coracoid process, is outlined. This communicates with the glenohumeral joint, where the articular cartilages on each side are seen as negative shadows between the medium and bone. The synovial reflexion along the intracapsular portion of the long head of biceps fills inferiorly to a level just below the transverse bicipital ligament, but no farther. The sub-acromial bursa, lying between the deltoid and the rotator cuff, does not fill unless the latter is torn. Such tearing was the most common lesion (70 cases) seen in this study, being the result of either recent trauma or slow degenerative attrition. Radiographically, the axillary view is particularly important, since abduction helps to force the medium through the defect. In 4 cases such tears were associated with tears of the long head of biceps, the contrast medium being seen to descend well down into the arm. Dislocation injuries cause ballooning of the capsule, and in cases of "frozen shoulder" the joint capacity is diminished. The authors consider the investigation to be of considerable value and hope to enhance its value still further by the use of cineradiography.

R. O. Murray

540. Left Retrograde Cardioangiography: Its Diagnostic Value in Acquired and Congenital Heart Disease

K. AMPLATZ, R. G. LESTER, R. ERNST, and C. W. LILLEHEI. *Radiology* [Radiology] 76, 393-401, March, 1961. 7 figs., 17 refs.

The authors describe their method of performing percutaneous transfemoral retrograde cardio-angiography which, they state, although admittedly not without its risks, is of undoubted value in the assessment of mitral and aortic valvular disease and also of certain congenital cardiac defects. At the University of Minnesota Hospitals, Minneapolis, more than 280 of these examinations have been carried out, with only 2 fatalities and several local complications. The usual Seldinger technique is employed, using a 260 polyethylene catheter with a curved tip and 4 or 6 side holes. The guide wire is left in the catheter until it is correctly positioned, with about 4 cm. of wire projecting. If difficulty is experienced in passing the aortic valve the curvature of the catheter can be altered by increasing or reducing the amount of extension of the guide wire. The concentrated contrast medium is injected under low pressure by a power injector, 40 to 45 ml. being given in 2 or 3 seconds and films taken in two planes at the rate of 5 per second, reduced to 3 per second after the injection. After filming this sequence the catheter is repositioned in the ascending aorta and a further 30 to 35 ml. of medium injected to test the competence of the aortic valve.

The appearances in mitral incompetence are described in detail (and some of them illustrated). Particular points made are that the catheter should be positioned near the cardiac apex, moderately slow injection of the medium should be employed, and serial films should be taken for at least 5 or 6 seconds. Increasing opacification of the left auricle is the most valuable sign of true mitral incompetence.

D. E. Fletcher

541. Aortography by Catheterization of the Right Atrium: a Safe and Reliable Method

A. ZERBI-ORTIZ and W. V. WELDON. *New England Journal of Medicine* [New Engl. J. Med.] 264, 19-23, Jan. 5, 1961. 8 figs., 21 refs.

A method of opacification of the thoraco-abdominal aorta and its major branches used at the Walter Reed General Hospital, Washington, is described as follows.

"Under local anaesthesia, a No. 8 to No. 10 National Institutes of Health Cardiac Catheter is placed in a peripheral vein and advanced into the middle of the right atrium under fluoroscopic control. A preliminary injection, containing sodium dehydrocholate and a test dose of 90% sodium diatrizoate, is made to determine the circulation time and sensitivity to the contrast material. The circulation time is used as an index of the time of appearance of the contrast medium in the arterial side of the circulation. The medium used is 90% diatrizoate in doses of 1.2 ml. per kg. body weight. Injection is accomplished by a compressed-air mechanical injector (Gidlund), which delivers the bolus of contrast material under a pressure of 10 kg. per square centimetre. Serial radiographs are taken in one or two planes with a Schönander Rapid Film Changer at a rate of one every

1½ seconds, bracketing the circulation time to cover 20 to 25 seconds."

This procedure was carried out in a total of 50 cases, in 9 of which occlusive disease of the carotid, vertebral, or subclavian arteries was demonstrated. No significant complications were encountered. The authors state that the hazards of direct aortic puncture are eliminated by this method. The difficulties of "rapidity of injection present in intravenous aortography are overcome by the use of the right atrium as the site of injection and the use of a mechanical injector".

The method is particularly suitable for the study of occlusive disease of the thoraco-abdominal aorta and its major branches, aneurysm formation, and renal hypertension, and for postoperative evaluation of vascular grafts.

J. MacD. Holmes

542. The Diagnosis of Aortic Coarctation in the Plain X-ray Film. (Zur Erkennung der Aortenisthmusstenose im Röntgennativbild)

F. LONGIN. *Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin* [Fortschr. Röntgenstr.] 94, 324-332, March, 1961. 10 figs., 24 refs.

Working at the Medical Polyclinic of the University of Würzburg the author has surveyed the radiographs in nearly 60 cases of coarctation of the aorta, and on the basis of his own and other authors' findings he concludes that a notch on the left outline of the aorta is an important piece of contributory evidence. In his experience notching of the ribs is present in two-thirds or more of all cases and, contrary to general belief, may occur as high as the second rib.

The following signs are present in between one-third and two-thirds of all cases: small or absent aortic knuckle, enlarged left ventricle (this is particularly telling in the young), dilated left subclavian artery, duplicated aortic knob and eventually high crested waves in the kymogram alongside the left subclavian artery and shallow crests alongside the descending aorta. The following are present in up to one-third of all cases: dilated ascending aorta, a prominent aortic knuckle, pre-stenotic aneurysm of the aorta, calcium deposits in a small aortic knuckle, displacement of the oesophagus owing to post-stenotic dilatation of the aorta, visible shadow of the internal mammary artery in the lateral view, notching on the neck of the scapula, a dilated and serpentine lateral thoracic artery in the lateral soft tissue of the thorax, and (of great importance) a notch on the left side of the descending aorta.

F. M. Abeles

543. Errors and Misconceptions in the Diagnosis of Gastritis. (Irrungen und Wurrungen in der Gastritisdiagnostik)

J. BÜCKER. *Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin* [Fortschr. Röntgenstr.] 94, 149-158, Feb., 1961. 7 figs.

Writing from Heidberg General Hospital, Hamburg, the author remarks that it is to be expected that there must be discrepancies between what is understood by gastritis as defined by the pathologist, the radiologist, and the gastroscopist. One of the main reasons for dis-

agreement is that it is known from the pathological findings that the deeper layers of the stomach, including even the serous coat, may be affected, but these are inaccessible to inspection by the gastroscopist and even a gastric biopsy specimen does not reveal the changes in the deeper layers.

In regard to radiological diagnosis, this also has its natural limitations. The main diagnostic feature is undoubtedly that resulting from oedema; this leads to coarsening of the mucous folds, which in order to be fully diagnostic, however, must remain stiff on pressure. The swollen folds are frequently an expression of the severe inflammatory oedema which affects all layers of the stomach and may increase the bulk of the wall of the organ to many times its original thickness. This oedema is of course capable of subsiding, when the folds may then regain their normal delicacy. In erosive gastritis, which is usually easily recognized radiologically, it is not so much the actual erosions which interest the radiologist but the over-all presenting picture. This is generally one of polypous gastritis, since the erosions lead to oedematous swelling which give to the gastric mucosa the appearance of rounded polypi; frequently these polypous swellings show a small, central, navel-like depression. Eventually these swellings, like the causative oedema, can also disappear. Sometimes erosive gastritis will lead to chronic gastritis.

F. M. Abeles

RADIOTHERAPY

544. The Implantation of Radioactive Isotopes (^{198}Au and ^{90}Y) into the Hypophysis in Metastatic Cancer of the Breast. A Clinical and Biological Study of 75 Cases. (L'implantation de matériel radio-actif intrahypophysaire (^{198}Au et ^{90}Y) dans les cancers du sein métastatiques. Bilan clinique et biologique à propos de soixante-quinze cas)

P. JURET and M. HAYEM. *Revue française d'études cliniques et biologiques* [Rev. franç. Ét. clin. biol.] 6, 19-34, Jan. [received March], 1961. 12 figs., 34 refs.

From the Institut Gustave-Roussy, Villejuif, France, the authors report the treatment of 75 patients with advanced cancer of the breast by the implantation of radioactive gold (^{198}Au) or yttrium (^{90}Y) into the pituitary fossa. In all cases the cancer was either fixed to the chest wall or already metastatic and was not suitable for further treatment by radiotherapy or hormones. Pituitary implantation was performed by the endonasal route using stereotactic localization. Treatment in 30 cases was by the insertion of 2 to 6 ^{198}Au sources with a total activity of 35 to 60 mc. and in 45 by the insertion of ^{90}Y sources—at first using 2 sources with a total activity of 12 to 16 mc., then some 60 sources totalling 5 to 10 mc., and most recently 4 to 16 sources totalling 7 to 12 mc.

After ^{198}Au implantation there was subjective improvement in 11 and objective improvement in 6 of the 30 patients. With ^{90}Y implantation there was subjective improvement in 29 and objective improvement in 16 of the 45 patients—in 6 of the latter group the results were spectacular and lasted over 3 months. Unilateral cranial

nerve lesions (2nd, 3rd, or 4th) occurred in 5 of 24 patients treated with less than 40 mc. of ^{198}Au and in all 6 patients in whom over 45 mc. of ^{198}Au was inserted. Of the 45 patients treated with ^{90}Y , 7 died within 30 days (4 from cancer), all developed diabetes insipidus, 3 developed cranial nerve lesions, and 5 had rhinorrhoea (2 with meningitis). The results of estimations of ^{131}I uptake, blood cholesterol level, and gonadotrophin and oestrogen excretion are reported in many cases.

It is considered that yttrium implantation is a valuable method of treatment, being considerably simpler than, although not yet as effective as, surgical hypophysectomy.

K. E. Halnan

545. Combined Therapy of Inoperable Lung Carcinoma with 5-Fluorouracil and Irradiation

F. M. WILLETT, L. V. FOYE JR., M. ROTH, and B. E. HALL. *Diseases of the Chest* [Dis. Chest] 39, 38-41, Jan., 1961. 3 figs., 6 refs.

Recent studies have suggested that 5-fluorouracil, a fluorinated pyrimidine, might potentiate the effects of radiation on tumour cells. The treatment of inoperable cancer of the lung with x-ray therapy or chemotherapy alone has been discouraging and unsatisfactory. Combined treatment has therefore been used in 16 cases of epidermoid carcinoma proved by biopsy.

Irradiation was given at 250 kV. (H.V.L. 3 mm. Cu) in daily tumour doses of 100 to 200 r. 5 days a week to a total of 2,000 r. 5-Fluorouracil was given on the first 4 days in doses of 15 mg. per kg. body weight (to a maximum of 1,000 mg.) daily and thereafter twice weekly in doses of 7.5 mg. per kg. (to a maximum of 500 mg. a day). The drug was given intravenously in 2 to 3 hours in 200 to 500 ml. of normal saline. The duration of treatment was 2 weeks. Five patients experienced no toxic symptoms, 7 had moderate pharyngitis and oesophagitis in the areas irradiated, and 4 developed leucopenia and 4 thrombocytopenia. All recovered, in none was treatment interrupted, and there were no deaths due to treatment. A response that could be measured objectively, either by palpation or radiography, occurred in all patients. This was both marked and rapid. One patient whose condition was considered terminal when treatment was undertaken was symptom-free and ambulatory 12 months later.

I. G. Williams

546. Lymphosarcoma: Survival and the Effects of Therapy

S. A. ROSENBERG, H. D. DIAMOND, and L. F. CRAVER. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [Amer. J. Roentgenol.] 85, 521-532, March, 1961. 9 figs., 32 refs.

A review has been completed of the experience at Memorial Center for Cancer and Allied Diseases [New York] with the group of diseases known generally as lymphosarcoma. All histologically proved cases were studied as of January 1, 1958, if they had been admitted to this institution between 1928 and 1953, thus providing a 5-year follow-up period. Histologic diagnoses were divided into three groups: giant follicular lymphosarcoma, 162 cases; lymphosarcoma, 553 cases; and reticu-

lum cell sarcoma, 554 cases. Patients with manifest leukemia when first seen at this institution were excluded. The age and sex distributions indicate a median age for the entire group of 49.7 years and a ratio of males to females of 1.7 to 1.

A leukemic transition was noted in 7.6% of the entire group and was related to the patient's age and the histologic classification. The objective and subjective response to treatment is presented for radiation therapy, 1,102 cases; alkylating agents, 326 cases; anti-metabolic drugs, 41 cases; adrenal steroids and/or ACTH, 158 cases; and radioactive phosphorus, 71 cases. The frequency of complications of therapy is also presented. Seventy-six patients who underwent radical surgery are compared to those with comparable disease who received non-surgical treatment.

The over-all 5-year survival rate, from clinical onset, of patients with lymphosarcoma is 28.4%. The median survival from clinical onset is 26.4 months. The survival figures as affected by the histologic group, age, sex, stage of disease, and year of admission are presented.

It is concluded that radiation therapy remains the treatment of choice for lymphosarcoma and that no increase in survival can be demonstrated over a period of 25 years, despite the addition of antibiotics, steroids, and alkylating agents to the therapeutic program of conventional radiation therapy.—[Authors' summary.]

547. The Effect of Cortisone during the Action of Ionizing Radiation on the Organism. (К вопросу о влиянии кортизона при воздействии на организм ионизирующей радиации)

M. JA. ČAJKOVSKAJA, M. P. ELEAZAROVA, V. B. ZAJRAT'JANC, and N. I. KARLAŠENKO. *Проблемы Эндокринологии и Гормонотерапии* [Probl. Endokr. Gormonoter.] 7, 20–29, Jan.–Feb., 1961. 7 figs., 23 refs.

It is well recognized that after irradiation noticeable changes occur in the adrenal glands. In the present investigation, carried out on 18 dogs and 150 rats to determine the effect of giving cortisone before and during intensive irradiation, 10 dogs received 15 mg. of cortisone every other day before irradiation and every 3rd day for 10 days after receiving a dose of 500 r.; the factors were 200 kV., 0.5 mA., distance 100 cm., and filter 0.5 mm. Cu and 1 mm. Al. The other 8 dogs, untreated, acted as controls. The rats received a dose of 700 r. and the 75 which received no cortisone again served as controls.

The urinary excretion of 17-ketosteroids increased in animals receiving cortisone, especially in those receiving it prophylactically. Changes in the blood picture occurred in all groups, but in those receiving cortisone these were short-lived and less severe. Animals were killed at varying intervals after irradiation and the adrenal glands examined histologically; the morphological changes in the glands were less severe in those which had received cortisone. Of the 10 dogs given cortisone, 6 showed a severe reaction, 4 a moderate reaction, and 3 died, while of the 8 controls, 6 showed a severe reaction, 2 a moderate reaction, and 4 died. The average survival period was 17 days in the former group, and 14 days in the latter. There is therefore

reason to believe that the administration of cortisone diminishes the sensitivity of the organism to intense irradiation, especially if treatment is begun before the exposure.

Cortisone was also given to 20 patients receiving deep irradiation for cancer of the oesophagus and lung, with the consequent likelihood of severe radiation sickness. The steroid enabled the course to be completed without interruption and prevented pulmonary complications.

L. Firman-Edwards

548. Comparison of Local and General Reactions to Various Types of High-energy Radiotherapy (^{60}Co , 2-MeV. Van de Graaff, and ^{137}Cs). (Raffronti fra reazioni locali e generali in vari tipi di radioterapia ad alta energia (Co^{60} , VAN DE GRAAF da 2 MeV e Cs^{137}))

R. MICELI, C. RIMONDI, and F. BONO. *Radiobiologia, radioterapia e fisica medica* [Radiobiol. Radioter. Fis. med.] 32, 421–436, 1961. 12 figs.

This paper from the University of Bologna summarizes observations made on patients treated with fixed fields—a single field, 2 opposed fields, or 3 cross-firing—by three different sources of high-energy radiation—cobalt (^{60}Co) beam (1.25 MeV.), Van de Graaff generator (2 MeV.), and caesium (^{137}Cs) beam (0.66 MeV.). Treatment with the first two was at 80 cm. distance and with the last at 40 cm.

On the skin the reaction from all three was always less than from 200-kV. deep x rays owing to the "build-up" effect, with the maximum dose at 1.4 mm. depth for 0.66 MeV. and 5 mm. for 2 MeV. With the Van de Graaff apparatus and the cobalt beam, delivering single daily doses of 200 to 250 r., erythema appeared at a dosage of 4,000 to 5,000 r. in 20 to 30 days; treatment doses of 100 to 150 r. produced later erythema. Deep erythema or desquamation of epithelium appeared at 6,000 to 7,000 r. Epilation set in before erythema, presumably owing to the depth at which the hair bulbs lie. With the caesium unit erythema appeared at 3,000 to 4,500 r. in 15 to 20 days; reactions to treatment with caesium were intermediate between those with deep x rays and those with 2-MeV. or cobalt beam therapy, but more nearly resembled the latter. Mucosal reactions paralleled those of the skin. Late sclerotic effects on the skin were sometimes found, especially on the abdomen of obese women, after 6,000 to 7,000 r. in 25 to 30 days with cobalt beam or 2-MeV. therapy.

Radiation sickness was always less than with deep x rays. Cobalt beam therapy caused a greater upset than 2-MeV. or caesium therapy; vomiting and diarrhoea hardly ever occurred except with the cobalt beam. Changes in the blood picture were seen mainly with cobalt beam and 2-MeV. therapy as the caesium unit was used mostly for treatment to the head and neck. After treatment to the thorax or abdomen changes in the erythrocyte count were insignificant, but there was a fall in leucocyte count, more pronounced with cobalt beam than 2-MeV. therapy.

Radiation with the Van de Graaff apparatus was thus found to be superior to cobalt beam therapy as regards both radiation sickness and blood changes, while the skin effects were similar.

J. Walter